MASTER OF SCIENCE

An Epidemiological Study of Diabetic Cataract in Scotland based on Electronic Health Record (GoDARTS dataset)

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An Epidemiological Study of Diabetic Cataract in Scotland based on Electronic Health Record (GoDARTS dataset)

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Declaration

I hereby declare that I am the author of this Thesis; that the work of which this thesis is a record has been done by me, and it has not previously been accepted for a higher degree. I also state that all references cited have been consulted by me personally and the conditions of the relevant ordinance and regulations have been fulfilled.

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Cheng Chang

Supervisor

Signed_____ Date_____

Weihua Meng

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List of Acronyms

VI - Visual Impairment

LOCS III - Lens Opacity Classification System III

OCGS - Oxford Clinical Cataract Classification and Grading System

AR - Araldose Reductase

QOL - Quality of Life

RCGP - Royal College of General Practitioners

NHS - National Health Service

GoDARTS - Genetics of Diabetes and Audit Research Tayside Study

BMI - Body Mass Index

SIMD - Scottish Index of Multiple Deprivation

SBP - Systole Blood Pressure

DBP - Diastole Blood Pressure

LDL - Serum Low-density Lipoprotein

HDL - Serum High-density Lipoprotein

Abstract

Background

As the leading cause of global blindness and visual impairment (VI) by World Health Organization in 2010, cataract has been becoming a substantial public health problem all over the world accounting for almost 40 million blind people in developed and developing countries. Cataract-related VI and other VI are becoming one of the biggest economic burdens in prevention and treatment. Among all risk factors for cataract, diabetes is one of the most significant ones and the population of diabetic patient is growing. There is few recent cataract epidemiology study which focus on diabetic population especially in developed countries.

Aim

To provide a brief report of prevalence of cataract in diabetic population and explore risk factors of diabetic cataract in a Scottish health board area.

Method

The data of 3279 diabetic subjects in this cross-sectional study were collected from The Genetics of Diabetes Audit and Research Tayside (GoDARTS) project. All data collected from participants are anonymously linked to their electronic health records with consent. Health records are from the Scottish Care Information-Diabetes Collaboration (SCI-DC) database and NHS database.

Results

The prevalence of diabetic cataract was 38.2% (95% confidence interval [CI], 36.5-39.9), and the age adjusted prevalence was down to 24% (95% CI, 22.5-25.5). Prevalence was higher for women than men (40.8% vs. 36.0%, Relative Risk [RR] =1.13, 95% CI 1.04-1.24), and higher for those with shorter duration of diabetes (less than 10 years) than those with longer duration (49.7% vs. 37.5%, RR=1.33, 95% CI,

1.14-1.54). The risk factors for any cataract were older age (years, Odds Ratio [OR] =1.080, 95% CI, 1.070-1.090), longer duration of diabetes (years, OR=1.033, 95% CI, 1.032-1.053), being in a richer family than the most deprived ones (OR, 1.306 for deprived group, 1.897 for middle, 1.718 for affluent group). For biochemistry factors, albuminuria ≥20 mg/L (OR=1.273, 95% CI, 1.077-1.504), higher serum low-density lipoprotein ([LDL], OR=1.440 for 2.03-2.50 mmol/L, OR=1.493 for >2.50 mmol/L). For protective factors, being a female (OR=0.816, 95% CI, 0.689-0.967), higher systole blood pressure (OR=0.991, 95% CI, 0.986-0.996), higher total serum cholesterol (OR=0.650 for 4.12-4.66 mmol/L, OR=0.624 for >4.66 mmol/L).

Conclusions

Nearly one fourth of the studied diabetic population had cataract, and there are neither evident risk factors nor protective factors for cataract in diabetic subjects that were inconsistent with factors for cataract in general population.

Introduction

1. Understanding of Cataract from Epidemiology and Public Health Perspective

The classic definition of public health is known as “the art and science of preventing disease, prolonging life and promoting health through the organized efforts of society”. [1] As time goes by, the meaning of public health has been broadened, the latest definition in terminology dictionary added “control of community infections, the education of the individual in principles of personal hygiene, the organization of medical and nursing service for the early diagnosis and preventive treatment of disease, and the development of the social machinery”. [2]

Visual impairment (VI) is one of the most concerned public health issues in the world and cataract is the second cause of visual impairment globally; also cataract accounts for more than half of world blindness. [3] Although most individual’s cataract are treated by surgery [4] but from public health practice perspective, more progress remains to be achieved.

Epidemiology is the fundamental scientific method or tool in public health practice. It is the study of certain disease in a defined population. An epidemiological research on cataract can not only contribute to health guideline making, medical practice or policy decision by exploring the distribution, prevalence, determinants of cataract from population perspective, but also be used in evaluating and measuring the efficacy of cataract-related public health actions. But the roles of epidemiology in public health remain controversial after years of widely applications. The results of epidemiology can only offer scientific knowledge but the how to put those conclusions into public health actions is still a matter for our researchers to think.

Current studies of cataract in public health field still focus more on epidemiology. Those studies are mainly observational ones, which means that they analysis the data collected from a certain population or a representative subset without intervention. By all means, for now it is the best way to contribute data to the knowledge of current stats of cataract among populations.

2. Understanding of Cataract and Diabetic Cataract

2.1 Definition and Classification of Cataract

Cataract is a visual impairment that causes opacity of the natural, crystalline lens of the eye due to opacification or optical dysfunction. It reduces the amount of incoming light and prevents a clear vision. [5,6] The definition of diabetic cataract is cataract that associated with diabetes mellitus.

Most of cataract cases are age-related but there are other types of cataract: traumatic cataract is cataracts that occur after an eye injury; secondary cataract occurs after surgery for other kinds of eye disease, or develop along with other health problems, such as diabetes; [7,8] congenital cataract is cataract which babies born with or develop later during childhood; radiation cataract develops after radiation exposure. These different types of cataract are classified by etiologic or potential causation, but the causes of cataract are complicated, and the types of cataract coexist. Besides the etiological classification method, cataract can also be classified by the degree and anatomical location of clouding within the lens (morphological classification) by utilizing grading systems like Lens Opacity Classification System III (LOCS III) and Oxford Clinical Cataract Classification and Grading System (OCGS).

For now, the most widely applied classification and grading method in epidemiology practice is Lens Opacity Classification System III, known as LOCS III. [9] It can distinguish the detailed type and density of the cataract by using slit-lamp and

retro-illumination pictures and comparing with standard photographic transparencies of lens of four types of cataract: nuclear color(NC), nuclear opalescence(NO), cortical cataract(C) and posterior subcapsular cataract(P). [10,11]

Another cataract grading method is the Oxford Clinical Cataract Classification and Grading System (OCGS). OCGS uses standard diagrams and Munsell color samples for the grading of nuclear cataract(NC), cortical cataract(C) and posterior subcapsular cataract(P).

Nuclear cataract(NC), cortical cataract(C) and posterior subcapsular cataract(P) are the three primary type of age-related cataracts. The meaning of each type is self-explanatory by its name. Nuclear means that the cloudy areas are in the central portion of the lens; cortical indicates that cloudy areas exist in the lens cortex, which is the peripheral edge of the lens and posterior subcapsular means opaque area on the back surface of the lens beneath the lens capsule.

2.2 Mechanism(pathogenesis) of Cataract and Diabetic Cataract

Generally speaking, the key mechanism in cataract is oxidation injury (oxidative stress) caused by peroxide free radical that lead to changes in the crystallins in the lens. Protein and lipid in the lens that experiencing extensive oxidation can affect the refraction and transparency of the lens, thus increasing visual opacity. [12]

A review article suggests that increasing oxidative stress is strongly associated with both types of diabetes and can accelerate the development of diabetes complications including diabetic cataract. [13] But in acute diabetic cataract model oxidative stress plays only a minor role in the opacification of lenses while chronic oxidative stress caused by polyol pathway is an essential factor during the development of long term diabetic cataract and other diabetic complications. [14]

The source of this oxidative stress was no longer unknown in the recent decade. The aldose reductase (AR) which catalyzes the reduction of glucose to sorbitol through the polyol pathway (AR pathway) is one of the most studied ones. [14,15] Osmotic stress is one of the hypothesis for diabetic cataract formation through AR pathway, suggesting that the intracellular increase of fluid in response to AR-mediated accumulation of polyols results in lens expansion and ultimately leading to cataract formation. [16-18]

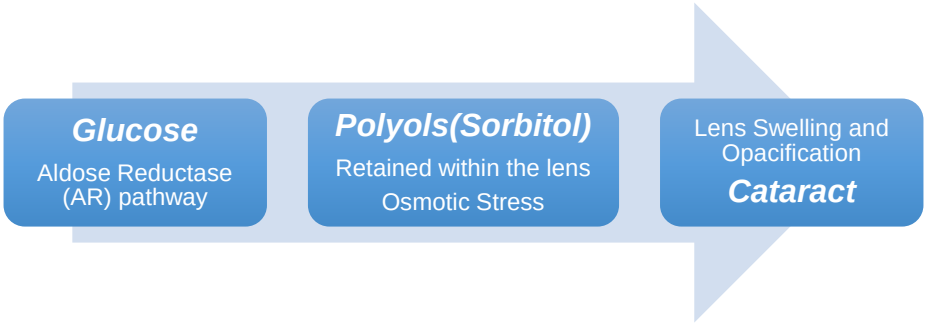

Figure 1. Pathophysiology of diabetic cataract formation

3. Prevalence of Cataract in Epidemiology Studies

Globally, the number of individuals who are visually impaired is "estimated to be 285 million, of whom 39 million are blind, with uncertainties of 10-20%". [3] According to the latest report from WHO on visual impairment, cataract is the leading cause of blindness (51%) and the second leading cause of visual impairments (33%). It is estimated that the prevalence of cataract in adults over 50 years of age was estimated at 47.8% and approximately, 90% of global cataract are in developing countries. [19]

There are many classic large-scale cohort studies on cataract such as the Wisconsin Beaver Dam Study, the Australian Blue Mountains Eye Study, the Barbados Eye Study, the French Pathologies Oculaires Liees a I's Age Study, and the West African Countries Study. [20-24] The current estimations of global cataract are mostly based on above studies.

3.1 North America, Europe

In a study conducted by The Diseases Prevalence Research Group in 2004, it is estimated that 20.5 million Americans older than 40 have cataract in either eye, and the prevalence of cataract in the US is 17.2%. The research group also provides an estimation of the total number of persons who may have cataract in the US by 2020. The predicted figure is 30.1 million. [25]

Another study in Canada provides the prevalence of visual impairment and blindness using WHO standard (39.9%). [26] According to another fact that there are one third of visual impairment and blindness are due to cataract and complicates, the crude prevalence of cataract in Canada is 13.1%. The author also states the prevalence estimates are "comparable to studies from Australia, the United States, and Europe" and the results are similar.

For Europe, there is a informative review article covering major eye diseases, suggesting that the crude prevalence of cataract in European adults in 2007 was 19.3%.[27]

In an epidemiology study from Italy in 1994, the prevalence of cataract was estimated to be: nuclear opalescence in 18.5%, cortical cataract in 12.9%, and posterior subcapsular cataract in 10.8%. [28] The POLA study in France in 1998 provided the prevalence of cataract among men and women, 24.1%, 29%. [23]

In recent years, very few epidemiological studies have been conducted in the UK that has focused specifically on cataract, let alone cataract in the diabetic population. One study worth mentioning is the North London Eye Study. [29] This population based, cross-sectional study examined 1547 eligible people. The prevalence of cataract (senile or cataract within aged population) causing visual impairment was 30% among which, 88% of the participants were not be able to get in touch with necessary eye

services. Also in this population based, cross-sectional study, cataract prevalence for people aged 65 and older is 36%, and noticeably, there aren't any similar observational studies based on GP registration record in recent decades.

There are other studies that only focus on senile cataract. The crude prevalence of cataract in a Finish study is 34% in people over 65 years old and 10% in whole cases, which is relatively lower than other countries. [30] Similar figures are presented in a Polish study: 20.44% in people over 60 years old, 12.10% in all patients. [31] A Spanish study suggests that prevalence of senile cataract (over 64 years old) was higher in men (69.50%) in women (65.50%), but the different is statistically significant (P>0.05), the prevalence in this study is relatively higher than other countries. [32]

3.2 Developing Countries

In a study focused on the exploring the prevalence of cataract for different types and in a Tanzanian population, the researcher included eligible individuals aged above 40 years old (3268 cases) and graded the lens using WHO Simplified Cataract Grading System. The prevalence of cataract (grade 1 or above in either eye) was 15.6% for NSC, 8.8% for CC, and 1.9% for PSC. The prevalence of all types of cataract increased with age: 1.7% for NSC, 2.4% for CC, and 0.4% for PSC among persons in their 40s and 59.2% for NSC, 23.5% for CC, and 5.9% for PSC for those 70 years and older (P= 0.0001 for all cataract types). [33]

An epidemiology study in Beijing had a very detailed results presentation in its article. [34] Among all 4439 subjects examined (all above 40 years old), the prevalence of nuclear cataract was 50.3% (95% CI: 48.8%–51.8%), and the overall prevalence of any cataract was 53.1% (95% CI: 51.6%–54.6%), increasing from 6.5% (95% CI: 5.2%–7.8%) in those subjects 40 to 49 years of age to 52.3% (95% CI: 47.4%–55.3%) in those who were 50 to 59 years of age, and to 97.8% (95% CI: 96.4%–99.2%) in those 70 years and older (P<0.001). Frequencies of any cortical cataract and any

subcapsular posterior cataract were 10.3% (95% CI: 9.4%–11.3%) and 4.3% (95% CI: 3.7%–4.9%), respectively. And in another study in Taiwan senile population (65 years old), the prevalence for any cataract was 59.2% (95% CI, 56.6%–61.8%). [35]

Another cross-sectional study in India randomly sampled people aged ≥60 years in villages in both north India and south India. The Age- and gender-standardized prevalence of cataract in studied population was 58% in north India (95% CI, 56%–60%) and 53% (95% CI, 51%–55%) in south India (P=0.01).[36] The prevalence for specific types of cataract were also calculated: The most common cataract was Nuclear cataract with the prevalence of 48% (95% CI, 46%–50%) in north India and 38% (95% CI, 37%–40%) in south India (P<0.0001) and figures for PSC were 21% and 17%; cortical cataract 7.6% and 10.2%. [36]

From above studies, it is worth noticing that cataract prevalence varies widely between studies from all over the world, the reasons for variation and difficulty for comparison among data could be the "differing population characteristics and diagnostic methods of lens opacity". [37]

4. Risk Factors of Cataract

Epidemiology studies on lens opacities focus mostly on age-related cataract, which means the population for these studies are mainly elder people. The reason is that age is the most distinct risk factor for cataracts, prevalence of any cataract or mixed cataract rises with elder age group. [23, 28, 30-37] In an evidence-based guideline for cataract surgery, the prevalence of cataract rose steadily with age: 16% in the 65 to 69 years age group, 24% in people of 70 to 74 years of age, 42% in those 75 to 79 years of age, 59% in those 80 to 84 years and 71% in people of 85 years or more. [38] Yet there are other widely acknowledged risk factors that were widely studied. Older age, women gender, and family history are classified into unmodifiable risk factors. [6] In

epidemiology practice, we adjust age and gender factors so that other potential modifiable risk factors can be explored.

According to an updated literature review, there are three main risk factors for senile cataract: smoking, UVB radiation exposure and diabetes mellitus. [19] These three factors have been frequently reported by multiple studies and reviews with adequate epidemiology and animal biochemistry evidence.

For smoking, "evidence shows a causal relationship between cigarette smoking and cataract." [39] It has been demonstrated by multiple studies that there was dose-effect relationship between pack of cigarette smoked and opacification degree and duration of smoking raised the risk of cataract. [40,41]

For UV-B light exposure, due to different exposure and outcome measurement, the relationship is not strong for all cataracts but only development of cortical cataract. [19] In a review of 22 epidemiology studies, most of the epidemiologic evidence support that the UV-B light exposure is a causality factor for cortical cataract. [42]

Diabetes is one of the most significant risk factors for cataract and the population of diabetic patients is growing. There is an increased prevalence of cataract in diabetic subjects compared with non-diabetic individuals. [43] According to the International Diabetes Federation's prediction, more than 285 million people have been affected by diabetes worldwide and this number is expected to reach 439 million by 2030. [44] In the famous Beaver Dam Study, result showed that diabetic patients were significantly "more likely to have cortical lens opacities" and were "more likely to have previous cataract surgery" than people without diabetes. Longer duration of diabetes also leads to a significant stronger probability of cataract. [20] Diabetes is also an important risk factor for other eye complications such as retinopathy, glaucoma. [45]

Besides those three key factors, there are other risk factors gathered and categorized in Table 1.

Table 1. Risk factors for age related cataract

	Risk factor	Higher risk/comment
Basic character	Age	Older
	Gender	Woman
	Race	Unclear, controversial
Personal condition	Diabetes	Longer duration
	Obesity	Higher BMI and wider waistline
	Hypertension (Cardiovascular disease)	
	Diarrhea	In some developing countries, controversial
	Myopia	Use of eyeglasses over 20 years
Medical side effects	Insulin	
	Corticosteroids	
	Cholesterol	
	Steroid	
	antioxidants	Controversial
Behavior	Smoking	Longer time, more cigarette
	Alcohol	More intake
Socioeconomic status	Occupation	Unprofessional
	Education level	Lower
	Income	Lower
Environment	Sunlight exposure	Longer, less protection

5. Impact of Cataract and Other Visual Impairments

5.1 Individual Impact

For individuals with visual impairments, the main outcome measure of impact on their life is through quality of life (QOL) questionnaires. Many vision-related QOL questionnaires has been developed that can help evaluate the impact of cataract and other visual impairments on patients. There are also generic QOL questionnaires such as EuroQol questionnaire (EQ-5D) which covers much wider aspects, however, a recent study suggests that the grading of visual impairment was only significantly associated with the score from vision-related QOL, but not with general QOL score determined by the EQ-5D. [46] So a vision-related QOL questionnaire is preferable in the field of ophthalmology.

Table 2. QOL dimensional structure, concept and impact on VI patients

Dimensions of QOL	Concept, meaning	Specific impact
Physical	Symptoms, treatment	Overall, eyesight, pain or discomfort around eyes
Functional	Self-care, mobility, activity level and activities of daily living	Reading difficulty（paper, street sign）, hard to find things, poor mobility in dim light or at night, driving difficulty
Social	Social contact, interpersonal relationships	Difficult to visit friends and going out have fun, influence working，hard to recognize people, accomplish less, financial pressure
Psychological	Cognitive function, emotional status, well-being, satisfaction and happiness	Feel need a lot of help and rely too much on others, depression, anxiety, embarrassment, frustration, worry, low self-confidence

There are four key dimensions that are introduced to classify all QOL-related concepts: physical, functional, social, and psychological. [47] Following this dimensional structure, specific impacts on VI patients are listed in Table 2.

5.2 Economic Impact

On one hand, cataract may bring about varied negative effects on patients' individual lives; on the other hand, cataract can have influence on society, especially on economy. Additionally, previous studies have proved that cataract-related and other VIs are some of the biggest economic burdens in prevention and treatment. In India, a study of direct and indirect economic loss due to blindness was carried out to estimate the burden of diseases and the benefit from interventions for prevention and treatment of blindness. The result showed the total cost was approximately Rs. 5.3 billion ($0.15 billion USD in the year 1996) for treating all cataract-related cases in India. [48] Another study on the economic burden of adult visual disorder in the United States found that the total direct medical cost in 2004 was $6.8 billion. [49] And recently, the global cost of VI (including VI caused by cataract) which consist of direct costs, indirect costs and health burden was estimated to be about $3 trillion USD in 2010 and was predicted to increase by 20% by 2020.[50]

An Australian study in 2006 provided a detailed report on economic impact and cost of visual impairment in Australia. [51] In 2004, visual impairments cost Australia about A$9.85 billion (approximately £5.24 billion), A$1.8 billion was spent on direct health system. The cost of VI is the seventh among all health system costs, ahead of VI is coronary heart disease, diabetes, depression, and stroke. Notably, cataract takes the largest 18% part of whole expenditure.

Table 3. Cost list of sight loss in UK in 2013

Cost type	Result
Healthcare costs – Total direct NHS expenditure on eye health	£2.64 billion
Primary care costs – Expenditure on providing primary eye care services, which includes NHS sight tests	£496 million
Inpatient costs – Expenditure on providing inpatient ophthalmology services	£536 million
Outpatient costs – Expenditure on providing outpatient ophthalmology services	£677 million
Cost of care – Cost of providing residential and community care to blind and partially sighted people	£370 million
Indirect costs – Total cost of unpaid care, reduced employment and other indirect costs to the UK economy as a result of sight loss	£5.3 billion

Table 3 is a factsheet about sight loss in UK provided a detailed list of cost in 2013. [52]

In the above table, except indirect costs, other costs combined are called direct costs. In 2013, UK spent about £12.1 billion on eye-related cares and services, NHS expenditure alone accounts for 21.8% of total cost. [52] The corresponding percentage for Australia healthcare system is roughly 18.2%. In this report, Direct NHS expense includes hospital care (inpatient admissions, outpatient appointments); eye relevant medications and prescriptions; and some NHS sight tests, and for primary care services, most of the money goes to NHS sight tests provision.

The indirect cost of blindness and visual impairments is estimated to be about £5.3 billion, an increase of over £200 million compared to estimates for 2012. The largest proportion of indirect costs is associated with informal care, which in most cases is unpaid care or support from family members, friends or neighbors. Higher unemployment rates and the cost of extra medications and equipment are also significant contributors in indirect costs. All those costs combined put a huge economic burden on society.

Another report gives detailed cost figure of UK health care system expenditure by county and by eye condition in the year 2008. [53] (Table 4, Table 5) Expenditure on cataract can't be calculated because some costs are lack of information. But the rough estimation of cost on cataract is over 470 million (adding up all known figure), it is over 22% of total cost, similar to the 2013 report.

Table 4. Health care system expenditure by country (2008 £million)

	England	Scotland	Wales	N.I.	Total
Hospital recurrent expenditure	490.69	57.1	31.59	13.34	592.74
Non-admitted expenditure	437.46	31.68	26.77	12.08	507.99
Prescribing expenditure	134.9	10.78	9.37	3.09	158.12
General ophthalmic services (GOS)	386.28	56.93	24.44	16.39	484.04
Expenditure associated with injurious falls	N	N	N	N	25.1
Research and development	N	N	N	N	13.99
Residential care and community care services	242.42	37.4	13.16	11.71	304.69
Capital and administration	N	N	N	N	58.22
Total					2,144.89

Table 5. Health care system expenditure by eye condition (2008 £million)

	AMD	Cataract	DR	GLCMA	RE	Other	Total
Hospital recurrent expenditure	37.99	334.66	78.63	14.60	13.81	113.05	592.74
Non-admitted expenditure	15.56	82.48	245.34	19.75	55.13	89.75	507.99
Prescribing expenditure	3.42	29.29	5.21	109.66	0.77	9.79	158.12
General ophthalmic Services (GOS)	7.93	23.98	11.16	11.52	424.75	4.70	484.04
Expenditure associated with injurious falls	N	N	N	N	N	N	25.10
Research and development	3.42	0.73	3.32	1.04	5.49	0.00	13.99
Residential care and community care services	N	N	N	N	N	N	304.69
Capital and administration	N	N	N	N	N	N	58.22
Total							2,144.89

6. Prevention, treatment and current state in health care system for cataract in UK

Currently, there is no proven intervention that can affectively prevent both the formation and progress of cataract. As mentioned in section 4, a lot of factors have been proven related with cataract. The incidence of senile cataract is associated with obesity but whether weight loss can effect on cataract or not remains to be studied. Similarly, smoking is one of the well-known risk factors of cataract, dose-effect on development of cataract has long been proven by multiple studies, but until now, the consequence of stopping smoking on cataract is still unknown.

Oxidative stress is a major cause of cataract development, basic science research has demonstrated antioxidants had protective effect on lens tissue, and in several observational studies, vitamin C supplement can decrease risk of cataract formation. [54] Some nutritional supplementation studies were carried out in the last decades suggesting that anti-oxidant vitamin supplements may prevent cataract. [55-58] Review of cataract prevention mentioned that there was one large interventional trial that "demonstrated a significant difference in participants treated with high-dose vitamin C versus placebo" while "a more recent interventional study did not replicate these findings". [54]

However, according to the latest factsheet provided by Royal College of General Practitioners (GCGP), there are alternative approaches that may alleviate patients' opacified vision who are not suitable for surgery or choose not to have. For example, avoiding direct exposure of sunlight by "wearing a hat, or/and sunglasses (with UV-B protection)" in sunny days; increasing brightness levels while reading; update to stronger lens.

With all that said above, for now, most cataracts are considered as not preventable. The method to reduce cataracts significantly is through proper treatment and the only effective treatment for cataracts is extraction of opacified lens. Through surgery,

visually impaired or blind cataract patient can restore sight to as normal as possible. With years of improvement in cataract extraction technic, it has become low risk, high benefit and cost-effective. [59]

In UK, cataract extraction is the most frequently operated surgery and the number of cataract operations increased from 247,847 in 2001/2 to 336,967 in 2011/12. (HSCIC) It is performed mostly on elder group, over 90% of patients were 60 years or older. The access to surgery in UK with NHS is usually within a waiting time of less than 3 months. In addition, geographic variations in cataract removal surgery rates is still evident [60] and a new concern is that over provision now have become an issue in certain areas in UK. [61,62]

Nowadays, microsurgical techniques and intra-ocular lens technology keeps getting better and more affordable, as a result, in the quality and accessibility of cataract extraction and post-operative rehabilitation has also continued to improve, thus, the growth of recommendations and demand for cataract surgery is inevitable and with increasing life expectancy, cases of cataract and the demand for surgery will likely to rise in the near future.

Objectives

Cataract is the cause of blindness in 40 million people globally. Diabetes is one of the most significant risk factors and the population of diabetic patients is growing. Yet there are few recent cataract epidemiological studies which focus on a diabetic population especially in developed countries. UK is a developed country with a publicly funded health care system referred to as the National Health Service (NHS) which covers almost all medical and surgery needs for UK citizens including cataract. With the growing senile population and longer life expectancy, the need for cataract treatment and prevention will continuously rise which will ultimately add burden to NHS.

With the benefit of electrical medical record combined with the database from the GoDARTS project, this epidemiological analysis became possible without any large scale questionnaire survey.

The goal of this study is to provide an updated report of the demographic data and the prevalence of cataract in a diabetic population and explore risk factors of diabetic cataract in Tayside health board area.

Methods

1. Introduction of Genetics of Diabetes and Audit Research Tayside Study (GoDARTS)

GoDARTS stands for "Genetics of Diabetes and Audit Research Tayside Study", this study is a quality resource that was initially funded by Wellcome Trust and supported by Diabetes UK. So far, there are three collections that consist of the GoDARTS database. All data in GoDARTS were collected from participants with consent. Patients gave informed consent to anonymously link their baseline data to their NHS electronic health records. The medical records include patient's prescribing history, general practice clinic visits, hospital admissions, and outpatient appointments. Furthermore, their personal information is anonymously linked with the Scottish Care Information-Diabetes Collaboration (SCI-DC) database. The consent also included anonymous retrospective and prospective follow up relating to diabetes from electronic medical records that were managed by the Health Informatics Centre (HIC) at the University of Dundee.

The core collection is Genetics of Diabetes Audit and Research in Tayside, which is a pilot study from January 1997 to October 2004; the second collection is Wellcome Trust Type 2 Diabetes Case Control Collection (WTCCC) which added Type 2 Diabetes case and control data into the database from October 2004-May 2009; and from October 2009, current collection continued to expand as WTCCC extension, the area covered are now including parts of Fife area.

So far, the dataset has more than 9000 consented patients with type 2 diabetes and over 8000 non-diabetics matching controls. Original data used in my project was updated until 2011, which consist of a total number of 10416 cases including patients with all types of cataract.

2. Literature research

The literature research consists of paper searching and reviewing which were for the purpose of background knowledge learning and information collecting. Because of the subject of this study belongs under one of the diabetic complications: cataract, my searching began with keywords as follows: cataract, visual impairment. Using these two core words combined with other keywords regarding to different aspects of my study was my overall searching strategy.

Review articles about cataract were first collected by using keywords “cataract” and “review”, and the latest review papers and some of their reference articles were carefully studied in order to have a general understanding of cataract including definition, classification, characteristic, pathobiology, etc. Then there were epidemiology studies and reports about cataract on a scale of regions, countries and even worldwide gathered from keywords searching “epidemiology”, “report”, “prevalence”, “risk factor”, “cataract” and “visual impairment”, by sorting out these papers, I got to know the prevalence of cataract in different regions and some of the key risk factors worth noticing.

Since the subjects in my dataset were all with diabetes condition, and my aim of this study is mainly to provide an updated report of cataract in a diabetic population and explore risk factors of diabetic cataract, articles concerning of diabetic cataract were separately searched with extra keywords: “diabetes”, “diabetic”, “diabetes mellitus” and “DM”. During this process, I found out that there has been no paper or report on diabetic cataract for the past two decades, which justified the rationality of my study.

3. Data Collection and Handling

Data were initially collected for my study in plain txt format. I imported all the data into SPSS so that all data files can be combined together with in one single file. Each

individual has a unique anonymous ID number, so that when combining two data files that included different aspects of patients e.g. biochemistry data, eye data, diabetes data, demographic data, blood pressure, deprivation and other miscellaneous data. Some of the raw data were calculated into new proper figures, such as duration of diabetes and BMI. The diabetes duration was a period from the date when a subject was first recorded or diagnosed with cataract till either the date the data was handled or the date the subject died before this study. A valid ID had to be presented in both files. If not, IDs and their representing case data shall be removed from collection.

Firstly, I combined all data files (excluding cataract related data) without any exclusion, and 10416 cases were included in my original collection. In this dataset, participants with all types of cataract, all ages or even missing some of phenotypic data. Since this is epidemiology study, there is no need to merge genotype data into my dataset.

The second step was to remove invalid cases with missing variables and/or outliner figures (e.g. age above 110 years) using the method above, cases with missing variables were excluded firstly in this step. From literature reviews about diabetes and cataract, I targeted people with the age of above 40 years with a history of Type 1 and Type 2 diabetes, and after removing all unqualified cases, a dataset of 7100 cases was created.

And the last step was to merge cataract data into my 7100 cases dataset. Before combining, the definition of a cataract case and a non-cataract case was necessary, in this study, a diabetic cataract case was defined as a diabetic patient (including type 1 and type 2 diabetes) who has had cataracts in at least one eye or cataract extraction surgery in at least one eye, according to linked e-health records. The subtype of cataract such as cortical, nuclear, posterior subcapsular cataract as well as the severity of cataract were not indicated in the e-health records, thus, the cataract case in the study referred to as any cataract case. The diagnosis of cataract was mainly made by

clinicians in the annual national retinal screen service. A non-cataract case was defined as a diabetic patient who has never been diagnosed with a cataract in the e-health records and has no cataract extraction surgery history.

When combining cataract data with 7100 cases dataset, 3821 cases removed because of lack cataract-related data (cataract eye, surgery eye information) or cataract status unknown. Finally, a dataset with 3279 cases in Tayside population was ready for further statistical analysis. The whole process of the any cataract group and non-cataract group (inclusion and exclusion) for analysis was organized in Figure 2.

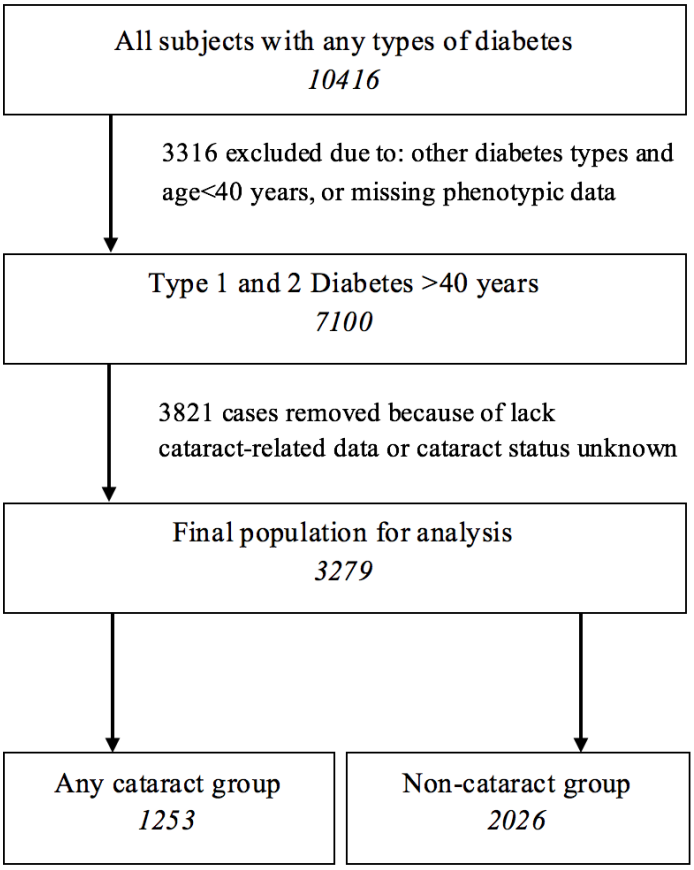

Figure 2. Process of any cataract group and non-cataract group (inclusion and exclusion) for analysis

4. Statistical Analysis

First, the prevalence of diabetic cataract was analysed and then the age-adjusted prevalence was calculated using adjusted age groups based on the Scotland Health Board Area 2006 census for the Tayside area. Prevalence for gender subgroups and duration of cataract subgroups (≤10 years and >10 years) were also analysed and compared using $\chi 2$ test, with $P<0.05$ indicating statistical significance. We then assessed baseline characteristics between the any cataract group and the non-cataract group by applying independent sample t-test for numerical variables and $\chi 2$ test for categorical variables. The risk factors for diabetic cataract were evaluated through both univariate analysis and multivariate analysis. Contingency tables were used for univariate analysis providing odds ratio (OR) for each risk factor with 95% CI. An is a measure of association between an exposure and an outcome. The OR represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure. For multivariate analysis, based on the review of general cataract, all variables included in the binary logistic regression model were pre-selected using enter mothed. And the regression was used to estimate the adjusted OR and test the possible association of other variables with diabetic cataract. We judged *P* values of 0.05 or less to be significant. All data handling and analysis were preformed using SPSS version 20. Geography figures were generated using Arcmap 10.3.

Result

1. Demographic Characteristics of Studied Participants

There were 3279 diabetic participants included for analysis, with either type 1 or type 2 diabetes and age above 40 years old. The mean age was 75.50 years with standard deviation of 11.23 years, the minimum age was 41 years and the maximum age was 101 years. In addition, among 3279 subjects, 46.2% were woman and 53.8% were man. Type 1 diabetes is relatively rare in the studied population with the percentage of 7.4% (95%CI: 6.6%-8.3%) compared to the more common type 2 diabetes (92.6%, 95%CI: 91.7%-93.5%).

1.1. Age

Table 5. Age group of all participants

Age group (Excluding upper limit)	Number of case	Percentage
40-50 years	76	2.3%
50-60 years	230	7.0%
60-70 years	610	18.6%
70-80 years	1043	31.8%
80-90 years	1046	31.9%
90 years above	274	8.4%
Total	3279	100.0%

People with the age of 40 years and above were included in this study and the minimum age was 41, the maximum age was 101. People with the age of above 65 years old were considered as senile individual with the percentage of 83.0%. Moreover, from the table and figure showing the age group distributions, it is clear

that the whole studied population was tend to be senile population. The most of the subjects were in the age group 80-90 years (1046, 31.9%) and the second most age group was 70-80 years (1043, 31.8%), followed with age group 60-70 years (610, 18.6%), age group 90 years and above (274, 8.4%), age group 50-60 years (230, 7%) and age group 40-50 years (76, 2.3%). In the bar chart of age group, the distribution was negatively skewed but the Q-Q plot indicated that the age distribution could be approximated as normal distribution. Because of the negative skew of the age group distribution, median age was used instead of mean age.

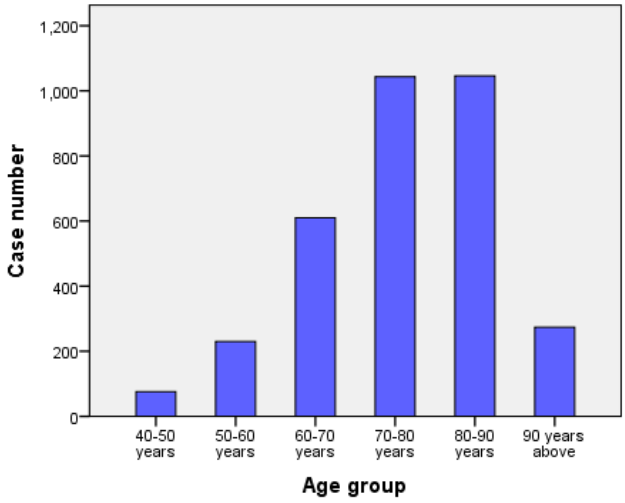

Figure 3. Distribution of participants by age group

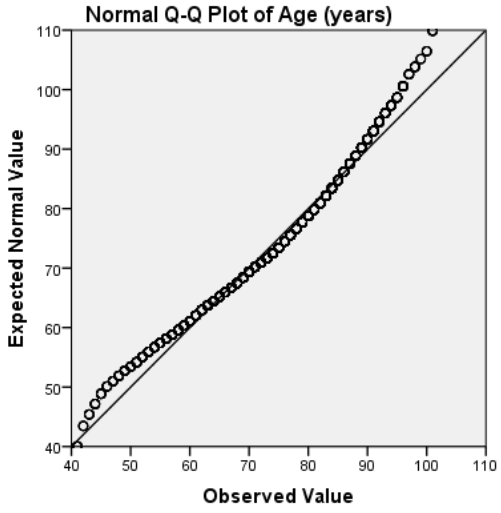

Figure 4. Q-Q plot of age

Table 6: Age by gender

Gender	Number	Median	1st Quartile	3rd Quartile	Std. Deviation
Woman	1516	78	69	85	11.70
Man	1763	76	68	83	10.78
Total	3279	77	69	84	11.23

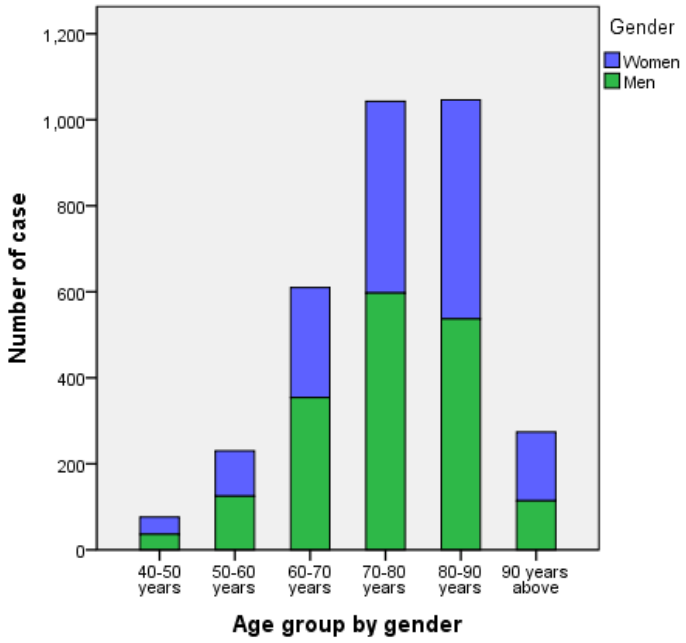

Figure 5. Distribution of participants by age group and gender

For these 1516 women, the median age of female was 78 years old and 76 years old for male. The median age of female and male among the general population of Scotland is lower than the studied population according to the 2006 Scotland's Census data.

1.2. Gender

Table 7. Gender distribution

Gender	Frequency	Percentage
Women	1516	46.2%
Men	1763	53.8%
Total	3279	100.0%

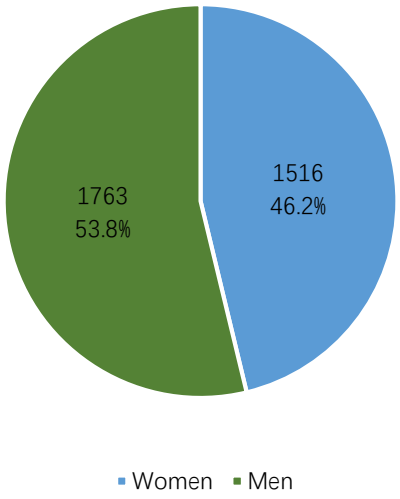

Figure 6. Pie chart of gender

Among 3279 subjects, 1516 were woman and 1763 were man. Female subjects contributed 46.2% of the total cases while male subjects contributed 53.8%. More female than male was in my collection of data.

1.3. Diabetes Type and History

Type 1 diabetes is relatively rare in the studied population with the percentage of 7.4% (95%CI: 6.6%-8.3%) compared to the more common type 2 diabetes (92.6%, 95%CI: 91.7%-93.5%).

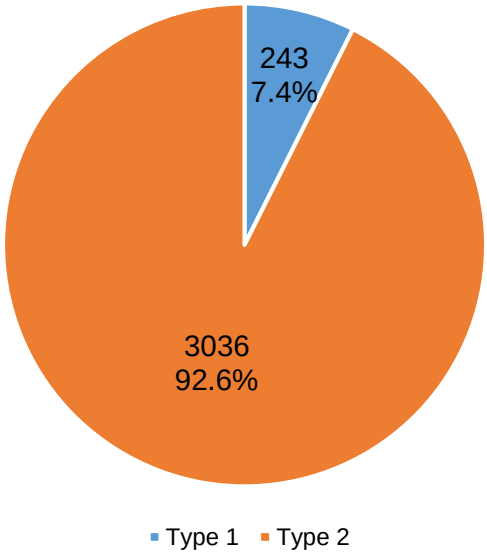

Figure 7. Pie chart of cataract type

And in terms of diabetes duration, the shortest diabetes history was 3 years and longest was 73 years, the mean duration of diabetes was 19.96 years with a standard deviation of 8.4 years. More than 90% percent of the included individuals had diabetes history of over 10 years while patients with diabetes of no more than ten years consisted of only 5.7% of the whole participants (Table 8). By looking into the frequency distribution of diabetes duration in Figure 8, I found that the histogram had a slight positive skew (skewness=1.56), the first quartile was 15 years, the second quartile was 18 years, and the third quartile was 27 years.

Table 8. Duration of diabetes

	Frequency	Percentage
Duration of diabetes, ≤10 years	187	5.7%
Duration of diabetes, >10 years	3092	94.3%
Total	3279	100.0%

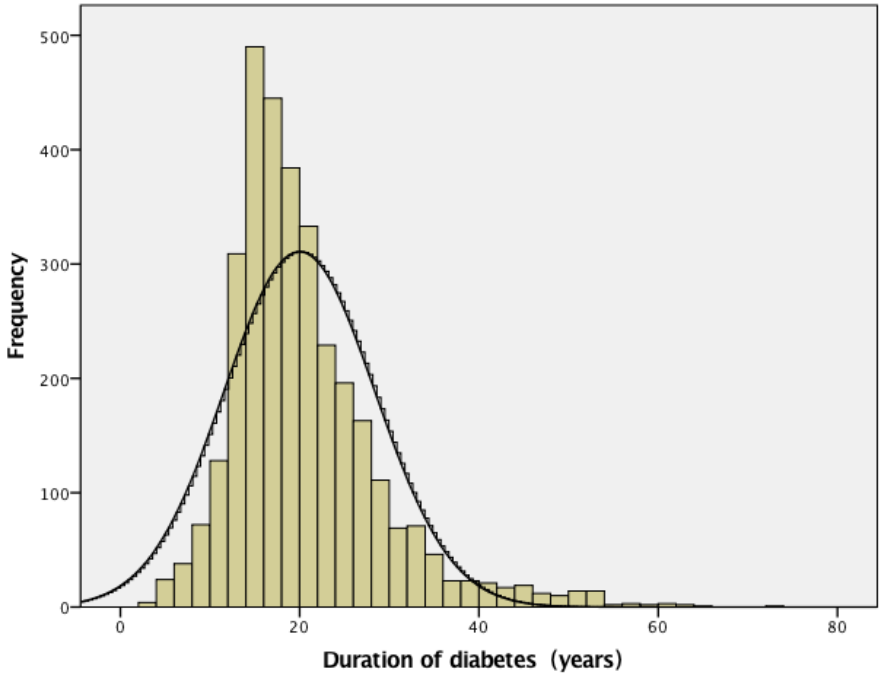

Figure 8. The histogram of diabetes duration (years)

1.4. Smoking

Table 9. Smoking status

Smoking status	Number	Percentage
Unknown	2	0.1%
Current smoker	448	13.7%
Ex-smoker	1173	35.8%
Non smoker	1656	50.5%
Total	3279	100.0%

Among 3279 subjects who had smoking status records, 448 (13.7%) were current smoker, 1173 (35.8%) were former smoker, 1656 (50.5%) never smoked. The length of smoking was not included in GoDARTS dataset.

1.5. Body Figure

The mean height of the population was 1.66 m, mean weight was 83.92 kg, and the body mass index (BMI) had the mean of 30.29 kg/m^2. If having BMI>25 kg/m^2 is defined as overweight, the prevalence for this particular population will be 80.2% (2631/3279). The gender difference can be observed from the box plot below (Figure 9), in this box plot, both women and men had similar level of BMI between the first quartile and the third quartile.

Table 10. Body figures

	Mean	Std. Deviation	Minimum	Maximum
Height (m)	1.66	0.1	1.34	2.00
Weight (kg)	83.92	19.75	34.90	191.80
BMI (kg/m^2)	30.29	6.44	13.63	64.09

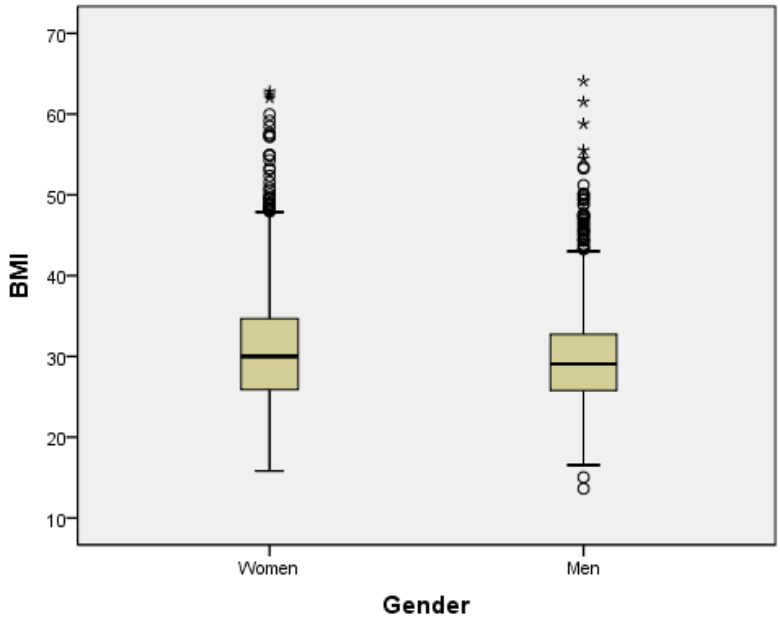

Figure 9. Box plot of BMI by gender

1.6. Deprivation Level

Deprivation Level in this study was defined using the SIMD (Scottish index of multiple deprivation) score which was based on the relative ranking from most deprived to least deprived. In this dataset, the relative ranking score was based in families within Tayside health board area. Deprivation level includes “most deprived”, “deprived”, “middle”, “affluent”, “most affluent” five levels.

Table 11. Deprivation level distribution

Deprivation level	Frequency	Percentage
most deprived	1046	31.9%
deprived	690	21.0%
middle	451	13.8%
affluent	444	13.5%
most affluent	648	19.8%
Total	3279	100.0%

In Table 11, it was worth mentioning that 31.9% of the participants were from most deprived families in Tayside health board area, and 21% were from deprived families, and these two combined consisted of more than half of the population.

1.7. Summary of Demographic Characteristics

Table 12. Summary of demographic characteristics

	Frequency or Mean	Percentage or SD
Age group		
40-50 years	76	2.3%
50-60 years	230	7.0%
60-70 years	610	18.6%
70-80 years	1043	31.8%
80-90 years	1046	31.9%
90 years above	274	8.4%
Gender		
Women	1516	46.2%
Men	1763	53.8%
Diabetes type		
Type 1 diabetes	243	7.4%
Type 2 diabetes	3036	92.6%
Duration of diabetes		
Duration of diabetes, ≤10 years	187	5.7%
Duration of diabetes, >10 years	3092	94.3%
Smoking status		
Unknown	2	0.1%
Current smoker	448	13.7%
Ex-smoker	1173	35.8%
Non smoker	1656	50.5%

Body figures		
Height (m)	1.66	0.1
Weight (kg)	83.92	19.75
BMI (kg/m^2)	30.29	6.44
Deprivation level (Tayside)		
Most deprived	1046	31.90%
Deprived	690	21.00%
Middle	451	13.80%
Affluent	444	13.50%
Most affluent	648	19.80%

To sum up, the studied population was a senile, overweighed group, with more than half of the individuals below middle deprivation level and almost 95% percent of diabetic patients had long-term (over 10 years) diabetes. The collected data contains a wide range of participants with different social background and clinical features to explore diabetic cataract from demographic perspective.

2. Medical and Biochemical Tests

Table 13. Characteristic of participants' medical and biochemical test results

	Mean or N	SD or %	95% CI
Blood pressure			
Diastole, mmHg	71.66	10.75	71.30-72.03
Systole, mmHg	136.71	18.78	136.07-137.36
Biochemical tests			
Total serum Cholesterol, mmol/L	3.97	0.98	3.94-4.00
Serum triglycerides, mmol/L	1.82	1.12	1.79-1.86
serum LDL cholesterol, mmol/L*	1.95	0.80	1.92-1.97
Serum HDL cholesterol, mmol/L*	1.28	0.41	1.27-1.29
HbA1c, mg%	7.74	1.59	7.68-7.79
Albuminuria			
<20 mg/L	2152	65.6%	64.0%-67.2%
≥20 mg/L	1127	34.4%	32.8%-36.0%

The diastole blood pressure (DBP) of the population was 71.66 mmHg ±10.75 mmHg (95% CI: 71.30 mmHg -72.03 mmHg), which lay in the ideal DBP range (60 mmHg-80 mmHg); the systole blood pressure (SBP) was 136 mmHg ±18.78 mmHg (95% CI: 136.07 mmHg -137.36 mmHg) which was between the interval for pre-high blood pressure (120 mmHg -140 mmHg)

The albuminuria test result showed 34.4% of diabetic patients had albuminuria more than 20 mg/L, which could indicate incipient diabetic kidney disease (more than 20 mg/L less than 300 mg/L).

3. Summary of Baseline Characteristics for Any Cataract Group and Non-Cataract Group

Table 14. Summary of baseline characteristics for any cataract group and non-cataract group

	Non-Cataract (n=2026)		Any Cataract (n=1253)		
	n(%) or Mean ± SD	95% CI	n(%) or Mean ± SD	95% CI	*P*
Age, y	72.51±11.07	72.03-72.99	80.38±9.67	79.84-80.91	**<0.0001**
Gender: Women	898(44.3)	42.2-46.5	618(49.3)	46.6-52.1	**0.005**
Duration of diabetes, y	19.04±7.24	18.72-19.35	21.47±9.84	20.92-22.02	**<0.0001**
Smoking					**0.021**
Non-smoker	1023(50.5)	48.3-52.7	633(50.5)	47.8-53.3	
Ex-smoker	680(33.6)	31.5-35.6	493(39.3)	36.6-42.1	
Current smoker	321(15.8)	14.3-17.4	127(10.1)	8.5-11.8	
BMI, kg/m^2	30.84±6.54	30.55-31.12	29.40±6.18	29.06-29.75	**<0.0001**
**Deprivation Level (Tayside) ** **					**<0.0001**
Most deprived	727(35.9)	33.8-38.0	319(25.5)	23.0-27.9	
Deprived	411(20.3)	18.5-22.0	279(22.3)	20.0-24.6	
Middle	237(11.7)	10.3-13.1	214(17.1)	15.0-19.2	
Affluent	241(11.9)	10.5-13.3	203(16.2)	14.2-18.2	
Most affluent	410(20.2)	18.5-22.0	238(19.0)	16.8-21.2	
Blood pressure					
Diastole, mmHg	72.60±10.54	72.14-73.06	70.16±10.92	69.55-70.76	**0.017**
Systole, mmHg	137.35±17.95	136.57-138.13	135.69±20.02	134.57-136.80	**<0.0001**
Biochemical tests					
Total serum Cholesterol, mmol/L	4.02±0.98	3.97-4.06	3.89±0.96	3.84-3.95	**<0.0001**

Serum triglycerides, mmol/L	1.88±1.15	1.83－1.93	1.74±1.05	1.68-1.79	**0.001**
serum LDL cholesterol, mmol/L*	1.96±0.82	1.93-2.00	1.92±0.76	1.88-1.96	**0.132**
Serum HDL cholesterol, mmol/L*	1.27±0.40	1.25-1.29	1.30±0.42	1.27-1.32	0.108
HbA1c, mg%	7.79±1.62	7.72-7.86	7.66±1.54	7.57-7.74	0.023
Albuminuria					**0.009**
<20 mg/L	1386(68.4)	66.4-70.4	766(61.1)	58.4-63.8	
≥20 mg/L	640(31.6)	29.6-33.6	487(38.9)	36.2-41.6	

*Differences not statistically significant between no cataract and any cataract group ($P \geq 0.05$)

**Deprivation Level (Tayside): the SIMD (Scottish index of multiple deprivation) score which was based on the relative ranking in Tayside from most deprived to least deprived. In this study, deprivation level includes “most deprived”, “deprived”, “middle”, “affluent”, “most affluent” five levels.

Table 14 presents the baseline characteristics of the study population between non-cataract group (n=2,026) and any cataract group (n=1,253). Only serum low-density lipoprotein (LDL) cholesterol and serum high-density lipoprotein (HDL) cholesterol were not significantly different between the non-cataract and any cataract groups ($P \geq 0.05$).

Compared to the non-cataract group, the any cataract group consisted of older participants (80.38 vs. 72.51 years), fewer female subjects (44.3% vs. 49.3%) and a longer history of diabetes condition (21.47 vs. 19.04 years).

For smoking status, the percentage of non-smokers are identical between the two groups (50.5%) while the non-cataract group had fewer ex-smokers and more current smokers than the any cataract group (33.6% vs. 39.3%, 15.8% vs. 10.1%). Surprisingly, BMI and blood pressure were higher for non-cataract group (BMI: 30.84

vs. 29.40 kg/m^2, diastolic blood pressure: 72.60 vs. 70.16 mmHg, and systolic blood pressure: 137.35 vs. 135.69 mmHg).

For deprivation level (The Scottish Index of Multiple Deprivation in Tayside), there was a pattern in both groups that, in the non-cataract group, patients were most likely to live in the both the most deprived and most affluent areas, while those in the middle categories were highest in the any cataract group.

For biochemistry variables, total serum cholesterol, serum triglycerides and HbA1c were all higher in the any cataract group (4.02 vs. 3.89 mmol/L, 1.88 vs. 1.68 mmol/L, 7.79 vs. 7.66 mg%). The high Albuminuria group (≥20 mg/L) had a higher percentage in the any cataract group than the non-cataract group (38.9% vs. 31.6%).

4. Results on Cataract Prevalence

4.1. Prevalence of Diabetic Cataract and Age-adjusted Prevalence

Table 15. Prevalence of diabetic cataract

	Prevalence			Age-Adjusted Prevalence*	
Cataract	n	%	95% CI	%	95% CI
Non-cataract	2026	61.8	60.1-63.5	76.0	74.5-77.5
Any cataract	1253	38.2	36.5-39.9	24.0	22.5-25.5
Total	3279	100		100	

*Age adjusted to population of Tayside, based on census of Scotland Health Board Area 2006

Table 15 shows that the prevalence of diabetic cataract is 38.2% (1253/3279), and the age adjusted prevalence is down to 24.0%. Prevalence of each cataract subtype are not reported due to lack of data in the initial record.

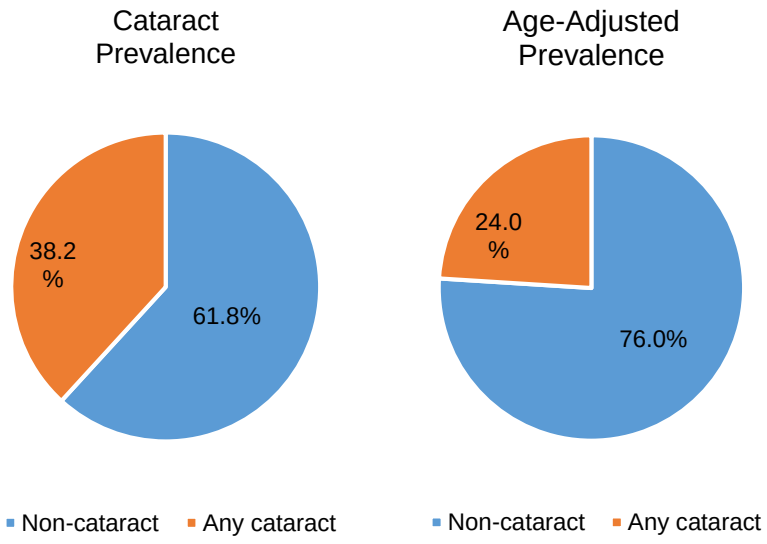

Figure 10 Prevalence of diabetic cataract pie chart

4.2. Prevalence of Diabetic Cataract by Different Subgroups

4.2.1. Diabetic Cataract Prevalence by Gender

The prevalence of diabetic cataract for women was 40.8% and 36.0% for men (40.8% vs. 36.0%, OR=0.818, 0.710-0.942 95% CI). The cross-tabulation result shows how any cataract and non-cataract individuals were distributed between different genders (Table 16). The Chi-square test revealed that the prevalence difference between female and male was statistically significant (P<0.05), and with OR=0.818, meaning that women had a lower chance of getting diabetic cataract than men.

Table 16. Cross-tabulation result for gender and cataract

	Female	Male	Total
Any cataract	618	635	1253
Non-cataract	898	1128	2026
Total	1516	1763	3279

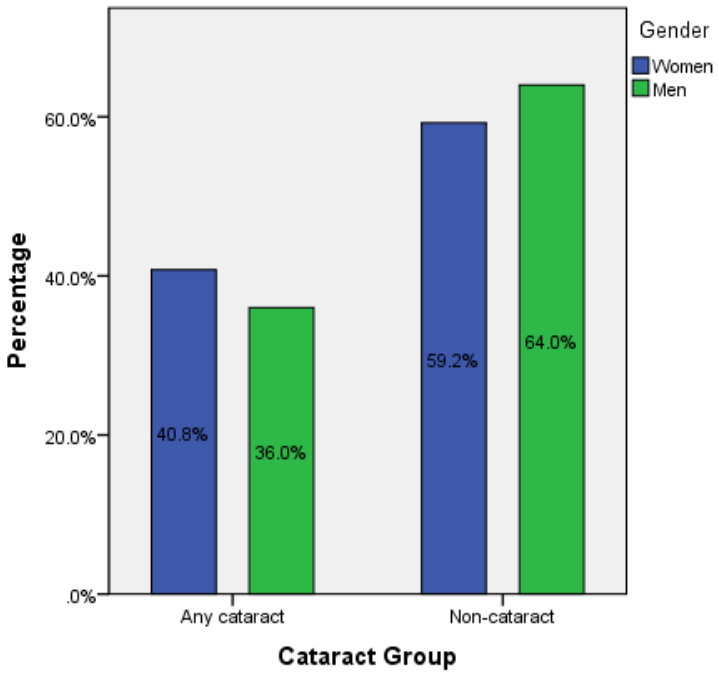

Figure 11. Prevalence of diabetic cataract in different gender bar chart

Figure 11 is a bar chart that describes the prevalence of diabetic cataract in different gender. There were less female diabetic cataract patients in quantity but the prevalence of diabetic cataract was higher for women.

4.2.2. Diabetic Cataract Prevalence by Age Group

The cataract prevalence for each age groups varied with statistical significance (P<0.05). 90+ years group has the highest prevalence of cataract 71.9%. 80-90 years group and 70-80 years group share a similar case numbers while the elder group has significantly higher cataract prevalence (51.6% VS. 35.2%). From Figure 12, the prevalence of diabetic cataract grows with age groups, as growing age can be a strong indicator for having diabetic cataract.

Table 17. Cataract and age group

	Age Group						
	40-50 years	50-60 years	60-70 years	70-80 years	80-90 years	90 years above	Total
Any cataract	11	40	98	367	540	197	1253
Non-cataract	65	190	512	676	506	77	2026
Total	76	230	610	1043	1046	274	3279

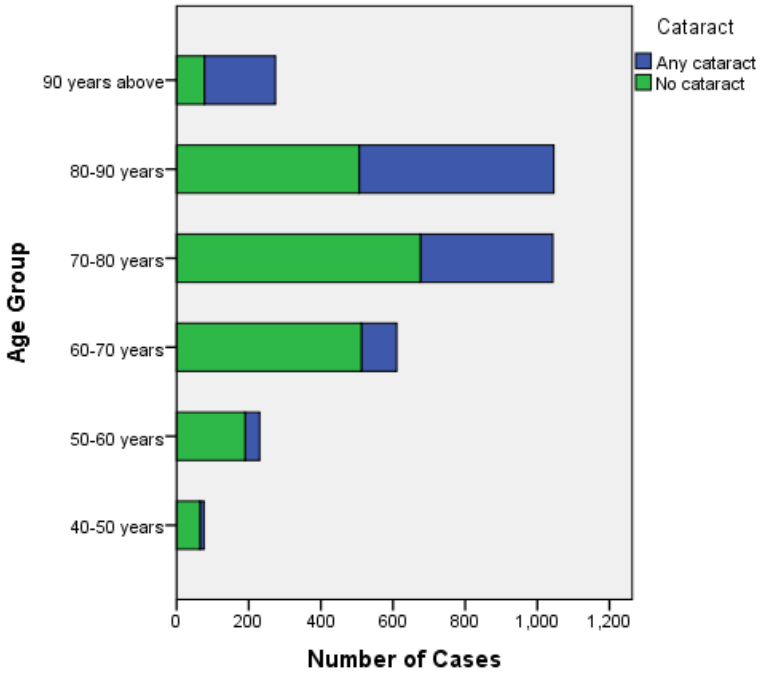

Figure 12. Prevalence of cataract in different age groups bar chart

4.2.3. Diabetic Cataract Prevalence by BMI (Overweight)

Table 18. Cataract prevalence by overweight status

	Over weight status		Total
	Normal Weight	Over Weight	
Any cataract	303	950	1253
	47.2%	36.0%	38.2%
Non-cataract	339	1687	2026
	52.8%	64.0%	61.8%
Total	642	2637	3279
	100.0%	100.0%	100.0%

An overweight subject in this study was determined by BMI of above 25 kg/m^2. There are 642 normal weight subjects and 2637 overweight subjects; the overweight rate is as high as 80.4%. The prevalence of cataract was 47.2% in normal weight group. However, the prevalence in overweight group was 64.0%. In Chi-square Tests, the difference between two groups is significant (P<0.05)

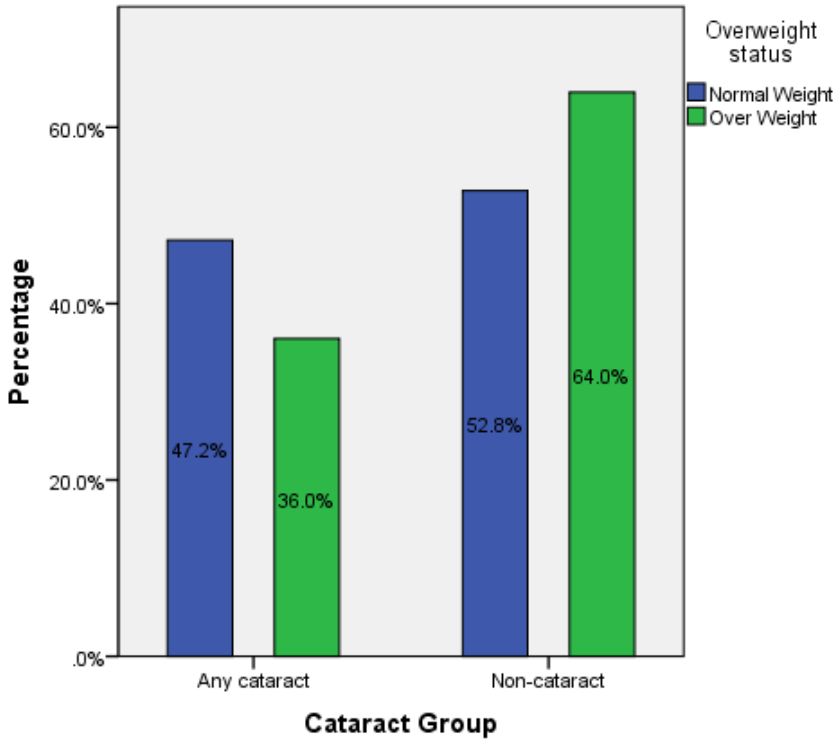

Figure 13. Prevalence of diabetic cataract by overweight or not bar chart

4.2.4. Diabetic Cataract Prevalence by Diabetes Duration

Table 19. Cross-tabulation result for duration of diabetes and cataract

	Duration of diabetes		Total
	Duration of diabetes, ≤10 years	Duration of diabetes, >10 years	
Any cataract	93	1160	1253
Non-cataract	94	1932	2026
Total	187	3092	3279

Although the percentage of diabetic cataract was higher for shorter duration (≤10 years) of diabetes compared to longer diabetes history (>10 years), and the chi-square test revealed that the prevalence difference between diabetes duration subgroups was statistically significant (P<0.05), it is not ideal to use categorical variable to explore its relationship with cataract compared to numerical variable. By exploring diabetes duration (years), the OR for diabetes duration was 1.035 with 95% CI of 1.026-1.044, which meant increasing in risk with increasing duration of diabetes.

4.2.5. Diabetic Cataract Prevalence by Smoking Status

Table 20. Cataract prevalence by smoking status

	Smoking Status				Total
	Unknown	Current Smoker	Ex-Smoker	Never	
Any cataract	0	127	493	633	1253
Non-cataract	2	321	680	1023	2026
Total	2	448	1173	1656	3279

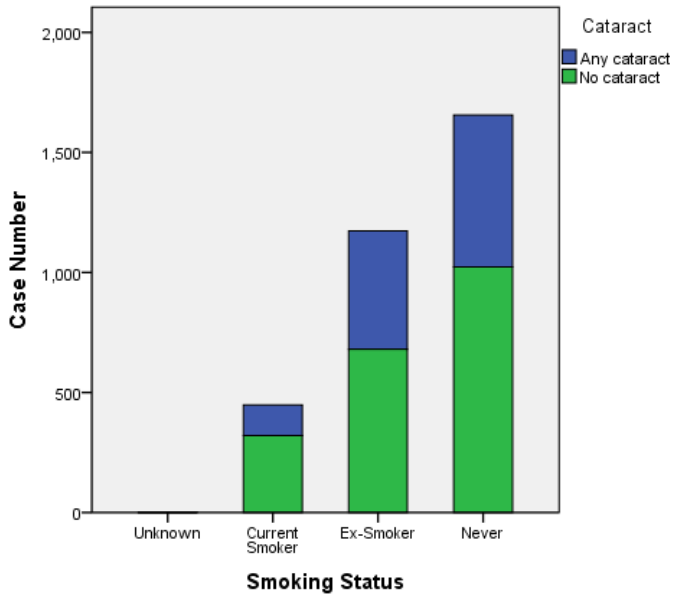

Figure 14. Distribution of diabetic cataract by smoking status bar chart

The results show that current smokers in the studied population have the lowest cataract prevalence (28.3%), and a non-smokers have the cataract prevalence of 38.2% and the ex-smokers have the highest cataract prevalence (42.0%).

4.2.6. Diabetic Cataract Prevalence by Deprivation Level

Table 21. Cataract prevalence by deprivation level

	Deprivation Level					
	most deprived	deprived	middle	affluent	most affluent	Total
Any cataract	319	279	214	203	238	1253
	30.5%	40.4%	47.5%	45.7%	36.7%	38.2%
Non-cataract	727	411	237	241	410	2026
	69.5%	59.6%	52.5%	54.3%	63.3%	61.8%
Total	1046	690	451	444	648	3279
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

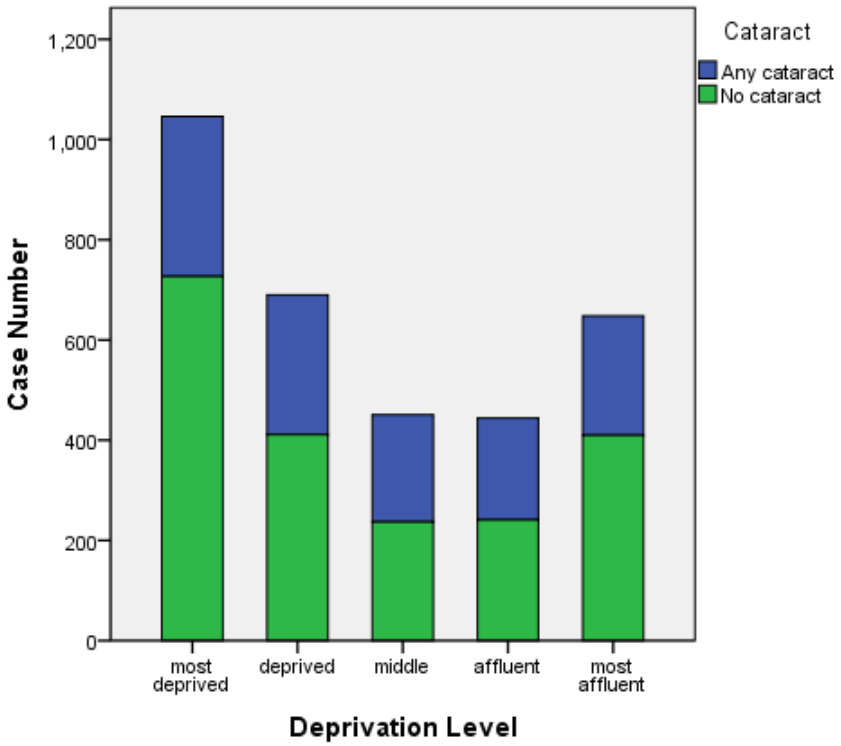

Figure 15. Distribution of diabetic cataract by deprivation level bar chart

Subjects from the most deprived families have the lowest cataract prevalence (30.5%) while the middle have the highest cataract prevalence (47.5%) followed by affluent (45.7%), these two groups also have the lowest number of subjects in the dataset. The Chi-square test shows that the cataract prevalence difference between different deprivation level was statistically significant (P<0.05).

5. Identification and Exploration of Diabetic Cataract Risk Factors

There are many known risk factors for general cataract and senile cataract, while the exploration of risk factors and protect factors has few supporting literatures. Based on the review of general cataract, selected variables were included in the binary logistic regression model using enter mothed.

Table 22. Risk factors for any cataract in diabetic subjects

	Univariate Analysis				Multivariate Analysis	
	n(%) or Mean ± SD Non-cataract (2026)	n(%) or Mean ± SD Any Cataract (1253)	OR (95% CI)	*P*	OR (95% CI)	*P*
Age, y	72.51±11.07	80.38±9.67	1.077(1.069-1.086)	**<0.0001**	1.080(1.070-1.090)	**<0.0001**
Gender						
Women	898(44.3)	618(49.3)				
Men	1128(55.7)	635(50.7)	0.818(0.710-0.942)	**0.005**	0.816(0.689-0.967)	**0.019**

Duration of diabetes, y	19.04±7.24	21.47±9.84	1.035(1.026-1.044)	**<0.0001**	1.043(1.032-1.053)	**<0.0001**
Smoking						
Non-smoker	1023(50.5)	633(50.5)				
Ex-smoker	680(33.6)	493(39.3)	1.172(1.006-1.365)	**0.042**	1.155(0.972-1.372)	0.102
Current smoker	321(15.8)	127(10.1)	0.639(0.509-0.803)	**<0.0001**	0.934(0.722-1.209)	0.604
BMI , kg/m^2						
1st quintile <25.06	343(17.0)	308(24.6)				
2nd quintile 25.06-28.04	397(19.6)	259(20.7)	0.727(0.583-0.905)	**0.004**	0.851(0.666-1.087)	0.196
3rd quintile 28.05-30.92	410(20.3)	245(19.6)	0.665(0.534-0.830)	**<0.0001**	0.842(0.655-1.081)	0.178
4th quintile 30.93-34.88	427(21.1)	230(18.4)	0.600(0.480-0.749)	**<0.0001**	0.883(0.684-1.139)	0.337
5th quintile >34.88	445(22.0)	210(16.8)	0.526(0.420-0.658)	**<0.0001**	1.023(0.781-1.339)	0.870
Deprivation Level (Tayside)*						
Most deprived	727(35.9)	319(25.5)				
Deprived	411(20.3)	279(22.3)	1.547(1.265-1.892)	**<0.0001**	1.306(1.047-1.629)	**0.018**
Middle	237(11.7)	214(17.1)	2.058(1.640-2.582)	**<0.0001**	1.897(1.477-2.438)	**<0.0001**
Affluent	241(11.9)	203(16.2)	1.92(1.528-2.412)	**<0.0001**	1.718(1.330-2.219)	**<0.0001**
Most affluent	410(20.2)	238(19.0)	1.323(1.076-1.627)	**0.008**	1.071(0.851-1.349)	0.559

Blood pressure						
Diastole, mmHg	72.60 ±10.54	70.16 ±10.92	0.995(0.992-0.999)	**0.017**	1.000(0.992-1.009)	0.970
Systole, mmHg	137.35 ±17.95	135.69 ±20.02	0.979(0.972-0.985)	**<0.0001**	0.991(0.986-0.996)	**<0.0001**
Albuminuria						
<20 mg/L	1386(68.4)	766(61.1)				
≥20 mg/L	640(31.6)	487(38.9)	1.377(1.188-1.595)	**<0.0001**	1.273(1.077-1.504)	**0.005**
Total serum						
Cholesterol, mmol/L						
1st quintile <3.16	363(17.9)	286(22.8)				
2nd quintile 3.16-3.66	402(19.8)	252(20.1)	0.796(0.638-0.992)	**0.043**	0.814(0.628-1.054)	0.119
3rd quintile 3.67-4.11	410(20.2)	248(19.8)	0.768(0.615-0.958)	**0.019**	0.789(0.597-1.044)	0.097
4th quintile 4.12-4.66	430(21.2)	229(18.3)	0.676(0.541-0.845)	**0.001**	0.650(0.479-0.881)	**0.006**
5th quintile >4.66	421(20.8)	238(19.0)	0.718(0.575-0.896)	**0.003**	0.624(0.446-0.874)	**0.006**
Serum triglycerides,						
mmol/L						
1st quintile <0.99	373(18.4)	284(22.7)				
2nd quintile 1.00-1.37	394(19.4)	263(21.0)	0.877(0.704-1.092)	0.240	0.913(0.711-1.173)	0.478
3rd quintile 1.38-1.80	417(20.6)	242(19.3)	0.762(0.611-0.951)	**0.016**	0.808(0.625-1.045)	0.104
4th quintile 1.81-2.44	410(20.2)	248(19.8)	0.794(0.637-0.991)	**0.041**	1.026(0.783-1.345)	0.852

5th quintile >2.44	432(21.3)	216(17.2)	0.657(0.525-0.822)	**<0.0001**	0.885(0.659-1.190)	0.419
Serum HDL cholesterol, mmol/L						
1st quintile <0.95	410(20.2)	253(20.2)				
2nd quintile 0.95-1.13	444(21.9)	216(17.2)	0.788(0.629-0.988)	**0.039**	0.688(0.534-0.886)	**0.004**
3rd quintile 1.14-1.30	395(19.5)	269(21.5)	1.104(0.885-1.376)	0.381	1.010(0.783-1.303)	0.939
4th quintile 1.31-1.58	402(19.8)	250(20.0)	1.008(0.807-1.259)	0.945	0.857(0.655-1.123)	0.263
5th quintile >1.58	375(18.5)	265(21.1)	1.145(1.917-1.430)	0.231	0.992(0.735-1.339)	0.959
HBA1C, mg%						
1st quintile <6.5	443(21.9)	301(24.0)				
2nd quintile 6.6-7.1	391(19.3)	243(19.4)	0.915(0.736-1.136)	0.420	0.951(0.748-1.208)	0.679
3rd quintile 7.2-7.8	413(20.4)	244(19.5)	0.870(0.701-1.079)	0.204	0.968(0.762-1.231)	0.793
4th quintile 7.9-8.9	358(17.7)	243(19.4)	0.999(0.802-1.244)	0.993	1.153(0.897-1.481)	0.267
5th quintile >8.9	421(20.8)	222(17.7)	0.776(0.624-0.966)	**0.023**	1.111(0.858-1.439)	0.423
Serum LDL cholesterol, mmol/L						
1st quintile <1.31	405(20.0)	257(20.5)				
2nd quintile 1.32-1.67	406(20.0)	260(20.8)	1.009(0.809-1.258)	0.935	1.244(0.969-1.599)	0.087
3rd quintile 1.68-2.02	410(20.2)	242(19.3)	0.930(0.744-1.	0.524	1.268(0.968-1.	0.084

			162)		661)	
4th quintile 2.03-2.50	388(19.2)	257(20.5)	1.044(0.836-1.	0.705	1.440(1.085-1.	**0.012**
			162)		912)	
5th quintile >2.50	417(20.6)	237(18.9)	0.896(0.716-1.	0.333	1.493(1.098-2.	**0.011**
			120)		030)	

Significant results are shown in bold front (P<0.05).

* Deprivation Level (Tayside) was the SIMD (Scottish index of multiple deprivation) score based on the relative ranking within Tayside from most deprived to least deprived. In this study, deprivation level includes “most deprived”, “deprived”, “middle”, “affluent”, “most affluent” five levels.

Table 22 is a summary table which includes the results of both univariate analysis and multivariate analysis of all variables. The analysis was performed to identify risk factors and protective factors for diabetic cataract. In the initial univariate analysis, the risk factors were older age (OR=1.077, 95% CI, 1.069), being female (OR=1.222, 95% CI, 1.061-1.408), longer duration of diabetes (OR=1.035, 95% CI, 1.026-1.044), being an ex-smoker (OR=1.172, 95% CI, 1.006-1.365) and being affluent (OR varied from 1.323 to 2,058). For biochemistry factors, albuminuria ≥20 mg/L (OR=1.377, 95% CI, 1.188-1.595) was the only identified risk factor, while other test results like higher total cholesterol (OR from 0.676 to 0.796), higher triglycerides (OR= 0.657 to 0.794) and higher HbA1c (5^{th} quintile OR=0.776, 95% CI, 0.624-0.966) were protective factors. It is worth noting that higher blood pressure (both diastole and systole) was a protective factor (OR=0.995, 95% CI, 0.992-0.999/OR=0.979, 95% CI, 0.972-0.985). Higher BMI (OR from 0.526 to 0.727) and being a current smoker (OR= 0.639, 95% CI, 0.509-0.803) were also unexpected protective factors.

In multivariate analysis, the risk factors for any cataract were older age (years, OR=1.080, 95% CI, 1.070-1.090), longer duration of diabetes (years, OR=1.033, 95% CI, 1.032-1.053) and being in an affluent family (OR, 1.306 for deprived group, 1.897

for middle, 1.718 for affluent group). For biochemistry factors, albuminuria ≥20mg/L (OR=1.273, 95% CI, 1.077-1.504) and higher serum LDL cholesterol (OR=1.440 for 2.03-2.50 mmol/L, OR=1.493 for >2.50 mmol/L) were risk factors. For protective factors, being female (OR=0.816, 95% CI, 0.689-0.967), higher systolic blood pressure (OR=0.991, 95% CI, 0.986-0.996) and higher total serum cholesterol (OR=0.650 for 4.12-4.66 mmol/L, OR=0.624 for >4.66 mmol/L) were identified.

6. Comparison of Risk Factors for Any Cataract in Gender and Diabetes Duration Subgroups

The analysis for gender and duration of diabetes on risk factors of diabetic cataract were presented in Table 23. It is worth noticing that albuminuria ≥20mg/L and diastolic blood pressure (DBP) were no longer significant in the population with shorter duration of diabetes, but given the fact that cataract patients with less than 10 years of diabetes is far less than those with longer diabetes duration (93 VS 1160), the I still consider albuminuria ≥20mg/L and lower DBP to be potential risk factors for diabetic cataract. HbA1c as a numeric variable was only significant in the female population as a protective factor.

Table 23. Differences in the risk factors for any cataract

	Gender		Duration of Diabetes	
	Men (635)	Women (618)	Shorter Duration (≤10 years) (93)	Longer Duration (>10 years) (1160)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age	1.070(1.059-1.082)	1.084(1.072-1.097)	1.102(1.060-1.145)	1.077(1.068-1.086)
Albuminuria ≥20 mg/L	1.409(1.154-1.720)	1.393(1.117-1.736)	1.383(0.774-2.472)*	1.362(1.169-1.586)
Diastole blood pressure (mmHg)	0.972(0.963-0.981)	0.986(0.977-0.996)	0.988(0.964-1.013)*	0.979(.0972-0.985)
Total serum cholesterol (mmol/L)	0.836(0.749-0.934)	0.869(0.784-0.964)	0.638(0.460-0.885)	0.898(0.832-0.969)
HbA1C (mg%)	1.002(0.940-1.068)*	0.898(0.842-0.958)	0.861(0.696-1.065)*	0.960(0.917-1.006)*

* P>0.05, not statistically significant.

7. Result on Postcode areas

7.1. Geographical Distribution of Diabetic Cataract Cases

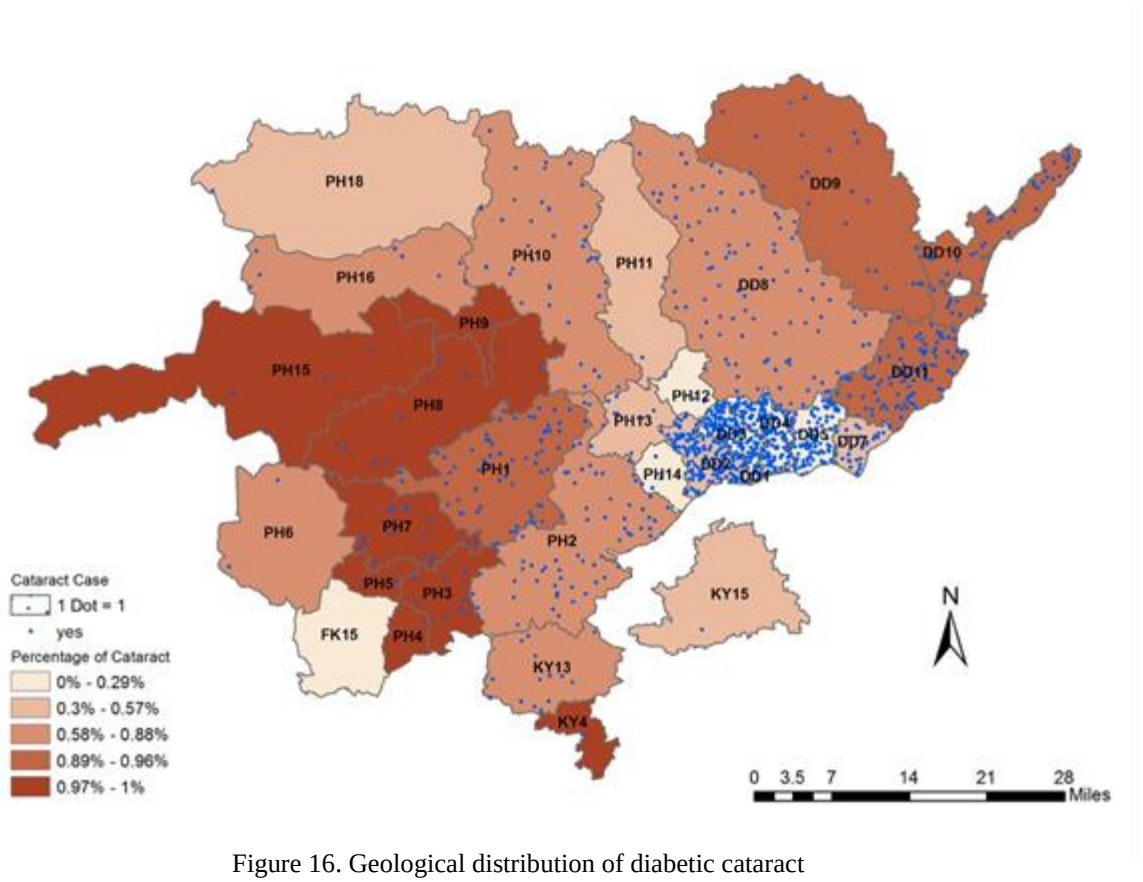

Figure 16. Geological distribution of diabetic cataract

Figure 16 shows the geographical distribution of diabetic cataract cases by postcode areas and the colour indicates the percentage of diabetic cataract case in each postcode area. Each blue dot represents one diabetic cataract cases, and from the map above, Dundee city had the most diabetic cataract cases but with lower percentage of cataract (number of cataract cases divided by whole population in the postcode area using 2006 census data) according to the light colour. In the city of Perth areas, the percentage of cataract is higher than Dundee city.

For diabetic patients, living in rural areas may have a higher risk of cataract compared to living in large urban areas, for example Dundee city (DD2-DD5) had the lowest

percentage of diabetic cataract cases (lighter colour) whilst DD7, 8, 10 and 11 (other urban areas) had a higher percentage (darker colour). Some rural postcode areas had only a few cases and the variation in their prevalence was large and unsuited for reference.

7.2. Diabetic Cases Percentage in Each Postcode Area

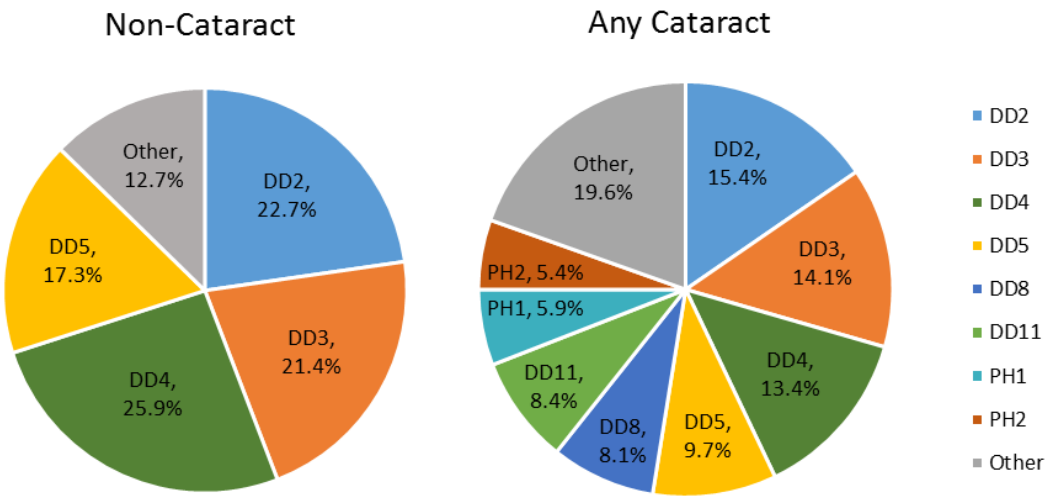

Figure 17. Diabetic cases percentage in each postcode area

Figure 17 shows the percentages of non-cataract and any cataract cases in each postcode area. 87.3% of non-cataract cases and 52.6% of any cataract cases were in Dundee city areas (DD2-DD5).

7.3. Result for Dundee City Areas

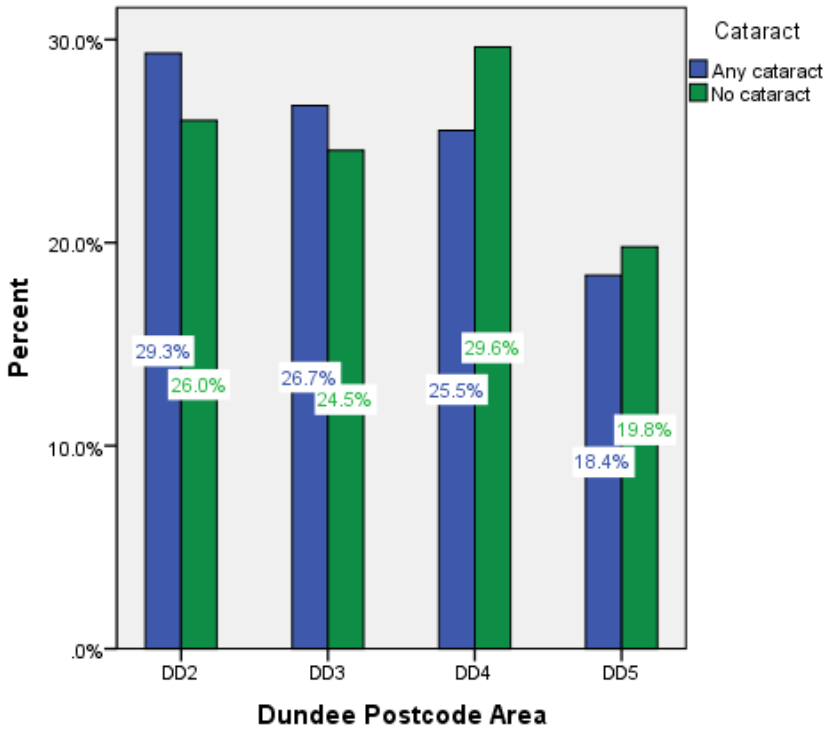

Figure 18. Prevalence of diabetic cataract in Dundee postcode areas

DD2 to DD5 postcode covers most areas of Dundee city from west to east. The prevalence of diabetic cataract for these postcode areas are showed in Figure 18. DD2 has the highest cataract prevalence 29.3% but still much lower than the overall cataract prevalence of the whole studied population. DD5 has the lowest prevalence (18.4%) in Dundee city area, but the Chi-square test result for postcode area and cataract had $P>0.05$ which means the difference between postcode is not statistical significant.

Then the following figures were created to reveal the distribution of deprivation status in different postcode areas.

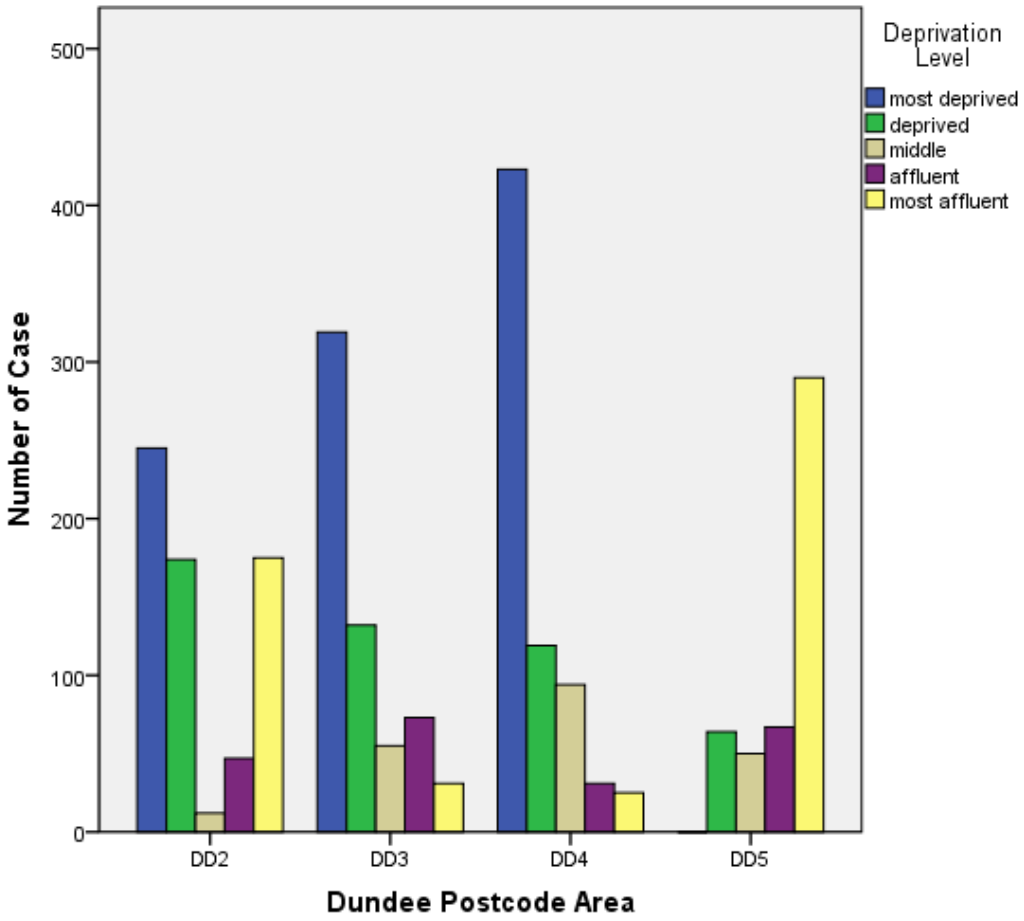

Figure 19. Distribution of subjects' deprivation level in Dundee postcode areas

DD5 has the most affluent individuals, followed by DD2 area, DD3 and DD4 have more poor families. Chi-square test shows that the difference of deprivation level is statistically significant ($P<0.05$). From the deprivation level in DD2 area, both the most deprived and most affluent individuals are dominant in this area. It became obvious that the weakness of using postcode area is that area divided by the first three digits of postcode is too large when analysing an area of high population density with complex component.

8. Geographical Distribution of Diabetic Cataract Cases

Table 24. Cataract related percentages

	Number of cases	percentage in any cataract group	Percentage in all cases
Current any eye cataract	976	77.9%	29.8%
Current single eye cataract	701	55.9%	21.4%
Current both eye cataract	275	21.9%	8.4%
Had any cataract extraction	277	22.1%	8.4%
Had only right eye extraction	58	4.6%	1.8%
Had only left eye extraction	150	12.0%	4.6%
Had both eye extraction	69	5.5%	2.1%

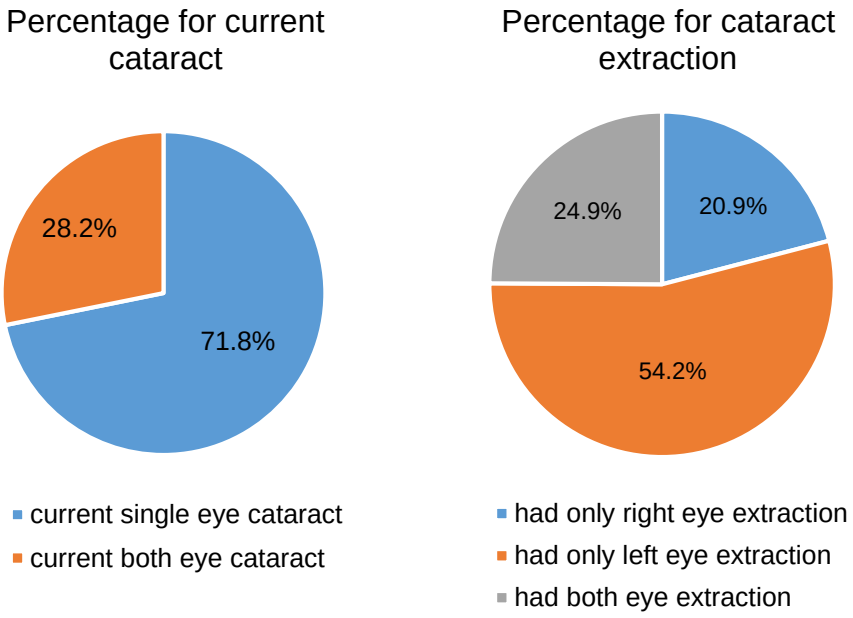

Figure 20. Pie chart of percentage for cataract eye and cataract extraction

Table 24 shows the distribution of diabetic cataract-related characteristics. Among 1,253 diabetic cataract cases, 55.9% (701/1253) of subjects currently had cataract in one eye and 21.9% (275/1,253) of subjects currently had cataract in both eyes, which was nearly one third of whole current cataract cases (28.2%, Figure 20). There were 277 (22.1%) diabetes cataract cases who had already had cataract extraction, among which, more than half of patients had left eye cataract extraction only (54.2%, Figure 20), 20.9% had right eye cataract extraction only (Figure 20) and a quarter of patients had extraction for both eyes (24.9%, Figure 20).

Table 25. Missing and unknown cataract eye cases

		Cataract Left Eye Case(N)				Total
		Unknown	Present	Absent	Missing	
Cataract Right Eye Cases(N)	Unknown	0	28	0	10	38
	Present	34	275	75	227	611
	Absent	0	57	2026	0	2083
	Missing	4	315	0	228	547
Total		38	675	2101	465	3279

The cross table for current cataract eyes shows that there are 10 cases with missing left eye data and unknown right eye data, and 4 cases with missing right eye data and unknown left eye data. With missing data and unknown status, the actual cataract and cataract surgery percentage for specific eye could not be known, the lack of detail in health record is one of the study dataset weakness.

Discussion

1. Discussion of the result

The purpose of this study was to explore the current diabetic cataract status in a certain health board area in Scotland (Tayside), using electronic health record linkage data, thus presenting an epidemiological report of cataract in a diabetic population over 40 years of age. Basic demographic variables, biochemical test results and medical results were all analyzed at different level. Risk factors and protective factors for diabetic cataract were also identified using regression models. The key finding of the study is that cataract (including who had cataract extraction) prevalence in a defined diabetic population is 38.2% (Table 15), and percentage of current cataract in this study is 29.8% (Table 24).

The prevalence data for different subgroups in this study (a diabetic population) were partially consistent with previous cataract studies' findings. In this study, I found that the prevalence of cataract in women was 40.8% compared with 36.0% of men. Similarly, previous studies for cataract prevalence in the United States and Australian populations reported that women had higher cataract prevalence and risk than men. [25,63]

Another result in this study showed that subjects who have had diabetes for less than 10 years had lower risk than patients with a diabetes history of over 10 years, which means that diabetic patients are more likely to develop cataracts with increasing diabetes duration. This result corresponded to previous findings in others studies where longer duration of diabetes was a significant risk factor for cataract and so the incidence of cataract would be expected to increase with longer duration of diabetes. [64] Furthermore, The Blue Mountains Eye Study 2-year follow-up found that diabetic patients with longer than 10 years' disease duration had a higher risk (RR=3.3) of

developing cataracts in the future. [65]

In Table 22, the multivariate analysis offered eight identified variables as risk or protective factors for diabetic cataract. We found that age and duration of diabetes were two strong non-modifiable risk factors. The main explanation is that lens proteins denature and degrade over time, and this process is accelerated by diseases such as diabetes. [65,66] We also noticed that the female gender tended to confer a protective effect (OR=0.846), however, females were proved to have a higher incidence of cataract than males by previous cataract studies. [67,68]

There was no clear cut for diagnostic criteria of hypertension in terms of blood pressure and thus the only cardiovascular related variable in this study was blood pressure number (diastolic and systolic). Based on a previous prospective study of blood pressure and risk of cataract, there was no strong association between cataract and blood pressure, which is subject to confounding by multiple risk factors. [69] However, recent findings suggest that cataract and systolic blood pressure were significantly associated but not associated for diastolic blood pressure. [70] According to the results, higher systolic blood pressure was a protective factor (OR=0.991), which would decrease 9.0% of risk when systolic blood pressure rose by 10 mmHg.

For biochemistry test variables, higher urine albuminuria (≥20mg/L) was a risk factor (OR=1.273), which can occur in patients with long-standing diabetes. [71] Findings from varied studies suggested that albuminuria predicted renal failure over the short and intermediate term. [72,73,74] As one of the severest complication of albuminuria, renal failure was identified as risk factor of cataract in a case-control study of cataract by Oxford University. [75]

In varied epidemiological studies, it has been suggested that in different contexts, cholesterol may act as an antioxidant in the lens. [76,77] Higher serum LDL cholesterol is another risk factor in this study (OR=1.440 for 2.03-2.50 mmol/L, OR=1.493

for >2.50 mmol/L), while results also showed higher total serum cholesterol to be a protective element (OR=0.650 for 4.12-4.66 mmol/L, OR=0.624 for >4.66 mmol/L). Previous study supported that High LDL cholesterol was a significant cataract risk factor. [78] The lens is supposed to be protected by the high HDL cholesterol, the low LDL: HDL ratio also could decrease the risk of cataract in patients. [79] However, no evidence was found that serum HDL cholesterol was significantly associated with the development of cataract.

We also included deprivation factors in the regression model that highlighted some interesting results. The SIMD score was introduced to measure deprivation level and it incorporated seven different aspects (employment; income; health, education, skills, and training; geographic access to services; crime; housing) of deprivation, combining them into a single index. SIMD score was based on ranking within a certain area. The SIMD scores we used were within the Tayside health board area. Previous studies have reported that more deprived populations have a higher risk of developing cataract. [80] Reports from the WHO Commission on Social Determinants of Health have emphasized the link between social and health inequalities. Lower socioeconomic status (SES) has been shown to be associated with a higher risk of eye health. [81,82] Affluent families are able to have access to better healthcare to help prevent cataracts from developing and they can even have cataract surgery at an early state of disease, which could reduce the prevalence of cataract. [82] In this study, being in a more affluent family than the most deprived ones increased the risk of cataract (OR, 1.306 for deprived group, 1.897 for middle, 1.718 for affluent group). The possible explanation could be that wealthier people in the Tayside area have a higher chance of being outside during leisure time and have higher UV light exposure. Another possible factor could be that the Tayside area includes some of the sunniest places in Scotland where the average is about 1,500 hours per year, which is more than the average in any other places (max 1,300 hours per year) in Scotland. [83] Consequently, people in the sunniest places tend to protect themselves from being exposed in the strong UV light damage that is recognized as a potential risk factor of

cataract. But as the limitation of using electronic records, the dataset from my study doesn't have information about UV exposure, so the real influence of sunshine exposure in the studied population remains to be further explored in the future. There is another reason related to accessibility, study showed that people with higher income were more likely to have eye screening services, [84] which may lead to a higher chance of being diagnosed with cataract. More studies are needed to explain why being affluent in the Tayside area is a risk factor for diabetic cataract.

The geological distribution of diabetic cataract cases was also presented in my analysis (Figure 16). Compared to living in city areas, living in rural places may lead to increased risk of cataract. On the one hand, people in large urban areas are more likely to have easy access to the healthcare system that offers some protection in disease. They are also more likely to have the resources and knowledge in cataract prevention. [85] On the other hand, though the cases in rural areas were fewer, large variation in the data existed. Residents in rural areas experienced higher risk of cataract and rural communities may have lower access to optometrists and other optical health tests. [86] The reason why the geological factor was not thoroughly analyzed was that the geological information was the first half of the postcode, which covered a relatively large area for each postcode area (e.g. area DD8, DD9). The deprivation level distribution in Dundee city area in Figure 19 showed that both the wealthiest and the poorest lived in DD2 area, which may hinder the representativeness of geological variable.

For the studied population, 29.8% of diabetic patients currently had cataracts in either eye. This included patients with single eye cataract (21.4%) and both eye cataract (8.4%) (Table 24). This is similar to previous reports that single eye cataract was worse than both eye, however, most people will eventually develop a cataract in both eyes, though one eye may be affected before the other. [87] Therefore, we could predict that the majority of patients with cataract are still in the process of cataract development. We also calculated the cataract extraction prevalence among studied

cases in Tayside (8.4%). Over the past decade, cataract surgical rates have doubled in most of UK. The current surgical rate approximates to a crude rate of 6.2 extractions per 1,000 populations. [87] The comparison with my results will show a consistent condition for surgery rate, because the surgery may be the only effective treatment for cataract for now. [87]

2. Contribution of the study

The key contribution of this study is presenting an update on current cataract epidemiological status by analyzing existing electronic health records. The major figures and trends are consistent with previous studies in sources of population-based data for the prevalence of cataract in the UK. The prevalence of visually impairing cataract rose steadily with age, especially 24.0% in people of 70 to 74 years of age compared with 35.2% in the people of 70 to 80 years old (Table 17). [29,88-91] The identification of several potential risk and protective factors for diabetic cataract can provide reference for future studies.

3. Shortcoming and limitation

One obvious shortcoming in this study was over exclusion of cases. To be more specific, I excluded diabetes cases with incomplete cataract information during data processing with a strict rule, any incompletion of information can lead to exclusion and the strict exclusion may lead to potential bias.

For instance, in the actual health record, according to previous findings concerning cataract duration, patients with shorter diabetes history were less likely to develop cataract and those who had no cataract tended to have incomplete cataract records (thus being excluded in the study). As a result, the number of non-cataract cases with shorter diabetes duration was likely underestimated in this study and the actual prevalence of cataract with less than 10 years' cataract history could be lower, and the

risk of longer diabetes duration can be underestimated. In previous studies, higher risk of cataract for the shorter diabetes duration patients may be expected if the association is attributable to the effects of poor vision because the level of VI would be better reflected by a recent eye examination than one performed years ago.

The major limitation of this study was the inability to subtype the cataract groups, which might invalidate some causal relationship between risk factor and cataracts or fail to identify potential risk factors. The other limitation is the lack of detail in cataract, cataract surgery and other medical record. Participants with healthy eyes have higher chance of being removed during data collection process. Address information is also limited to a vague postcode area which may hinder the research value from geographic perspective.

Another limitation was that since this is a cross-sectional study about a relatively chronic disease, the incidence of diabetic cataract can’t be properly calculated. And as a result, all risk values were measured in OR rather than RR, which made it difficult to interpreted directly.

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